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GONORRHEAL VAGINITIS IN GIRLS TREATED WITH ESTRONE (THEELIN), FEVER AND SULFANILAMIDE

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The methods employed until 1933 in the treatment of gonorrheal vaginitis [1] in children were largely those recommended for the treatment of gonorrhea in adults. For many years treatment with various antiseptics and gonococcocides was in vogue. They were applied in baths, douches, instillations, suppositories and ointments. Later there was added parenteral therapy, with vaccines, filtrates, nonspecific proteins, etc. Each method had and still has its ardent adherents; but in the hands of the majority of pediatricians and gynecologists the results have been disappointing.

Recently three new methods of treatment have been advocated, each attacking the problem from a different angle and each with the claim of a previously unheard of efficiency.

1. The first method consists of treatment with estrogens or with substances which produce an acid reaction in the vagina. The two types of medicament seem to be closely related in their mode of action. Estrogens administered to immature female monkeys [2] and human beings [3] change the vaginal epithelium from the infantile to the adult type. The infantile vagina is covered by a delicate epithelium measuring four to eight cell layers in thickness. The vaginal epithelium of the adult, and similarly that of the newborn infant,[3c] consists of twenty to thirty cell layers. These adult cells are characterized histologically

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1. The term "vaginitis" is used in this paper because of its shortness and widespread adoption. It is meant to include all gonococcic infections of the urogenital tract in girls.

2. Allen, E.: J. Morphol. **46**:479, 1928.

3. (*a*) Hartman, C. G., and Kuttner, A. G.: Anat. Rec. (supp.) **58**:68, 1934. (*b*) Lewis, R. M.: Am. J. Obst. & Gynec. **26**:593, 1933; (*c*) **29**:806, 1935.

by two qualities not present in the infantile cells: keratinization and storage of glycogen. With these facts in mind, Lewis [3b] in 1933 used theelin (estrone) for the treatment of gonorrheal vaginitis. The results appeared to be brilliant. And at that time he attributed the beneficial effect of estrogens to the mechanical protection of the vagina by the histologic changes just described. Subsequent studies [4] showed that with administration of theelin the p_H of the vaginal fluid changes from 7.0 - 7.2 to 4.5 - 6.0. Cruickshank [5] pointed out that this acid is lactic acid, produced by Döderlein's vaginal bacillus, which ferments glycogen. These studies point to the vaginal acidity as the most important part of the treatment with estrogens, since the gonococcus is known to be extremely sensitive to changes in the hydrogen ion concentration of its environment. These conclusions receive further support from the good results obtained with acid douches or with vaginal tablets containing weak acids or fermentable carbohydrates.[6]

Estrogens have been used widely during the last four years. The results of other authors, summarized in 1936 by a committee for survey of research on gonorrhea [7] and in 1937 by Benson and Steer,[8] will be referred to later in this paper.

2. The second new method is the treatment of gonorrhea with fever. Carpenter and his associates [9] reported in 1933 on the thermal death time of gonococci. Relying on their work and on some earlier suggestive clinical observations, Desjardins, Stuhler and Popp [10] developed a method for the treatment of gonorrhea with fever. They perfected their procedure within a short time, so that in 1936 [11] they claimed for their method an efficiency of 90 to 95 per cent in adults. Their results have been confirmed, and lately the method has been further improved.[12]

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4. (*a*) Hall, B. V., and Lewis, R. M.: Endocrinology **20**:210, 1936. (*b*) Lewis, R. M., and Adler, E.: Gonorrheal Vaginitis: Results of Treatment with Different Preparations and Amounts of Estrogenic Substance, J. A. M. A. **106**: 2054 (June 13) 1936.

5. Cruickshank, R.: J. Path. & Bact. **39**:213, 1934.

6. Karnaky, K. J.: Arch. Pediat. **54**:34, 1937. Little, A. A.: J. Pediat. **10**:202, 1937.

7. Vonderlehr, R. A., and others: Am. J. Syph., Gonor. & Ven. Dis. **20**:9, 1936.

8. Benson, R. A., and Steer, A.: Vaginitis of Children: Review of the Literature, Am. J. Dis. Child. **53**:806 (March) 1937.

9. Carpenter, C. M.; Boak, R. A.; Mucci, L. A., and Warren, S. L.: J. Lab. & Clin. Med. **18**:981, 1933.

10. Desjardins, A. U.; Stuhler, L. G., and Popp, W. C.: Fever Therapy for Gonococcic Infections, J. A. M. A. **104**:873 (March 16) 1935.

11. Desjardins, A. U.; Stuhler, L. G., and Popp, W. C.: Fever Therapy for Gonococcic Infections, J. A. M. A. **106**:690 (Feb. 29) 1936.

12. Warren, S. L.; Scott, W. W., and Carpenter, C. M.: Artificially Induced Fever for Treatment of Gonococcal Infections in the Male, J. A. M. A. **109**: 1430 (Oct. 30) 1937.

Spekter and McBride in a recent article on fever therapy in children [13] reported 5 cases of vaginitis treated with fever. Cures were obtained in 4 cases. The treatment of the fifth patient had to be discontinued because of convulsions. Schnabel and Fetter [14] obtained cures in 15 cases. Local treatment with diathermy had previously been used by Crossen.[15] Prolonged treatment gave favorable results.

3. The latest method of treatment is the administration of sulfanilamide. Dees and Colston [16] were the first to report the favorable action of this drug on gonorrheal infections of men. Only preliminary reports [17] on a total of 19 cases of gonorrheal vaginitis have been published. Of these cases, in 12 the condition was apparently cured, in 1 it recurred and in 7 it was unaffected.

The mode of action of the drug is not yet fully understood. It appears that the bactericidal action of sulfanilamide on streptococci (Bliss and Long,[18] Domagk [19] and others) and on gonococci [20] cannot account for the results obtained in animal experiments and in clinical experience.

This study has been undertaken with the hope of evaluating the individual merits of each of these three newer methods of treatment and of comparing their relative efficiency.

The comparison of results obtained by different authors with different methods may be misleading. This is due, as recently pointed out,[8] first to the lack of generally accepted standards for diagnosis and cure and second to the lack of uniformity of the case material, of the home environment of the patients and of the possibilities for check-ups.

Those conditions have been rather uniform in our institution during this study. We hope that this fact may justify the publication of results obtained with comparatively small groups and with short periods of follow-up.

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13. Spekter, L., and McBride, A.: J. Pediat. **11**:499, 1937.

14. Schnabel, T. G., and Fetter, F.: Am. J. Syph., Gonor. & Ven. Dis. **22**: 39, 1938.

15. Crossen, R. C.: J. Pediat. **6**:82, 1935.

16. Dees, J. E., and Colston, J. A. C.: Use of Sulfanilamide in Gonococcal Infections: Preliminary Report, J. A. M. A. **108**:1855 (May 29) 1937.

17. (*a*) Hagerman, P. O.: J. Pediat. **11**:195, 1937. (*b*) Carey, B. W.: ibid. **11**:202, 1937. (*c*) Lewis, R. M., and Adler, E.: Endocrine Treatment of Vaginitis of Children and of Women After the Menopause, J. A. M. A. **109**: 1873 (Dec. 4) 1937.

18. Bliss, E., and Long, P. H.: Observations on the Mode of Action of Sulfanilamide, J. A. M. A. **109**:1524 (Nov. 6) 1937.

19. Domagk, G.: Ztschr. f. klin. Med. **132**:775, 1937.

20. Cohn, A.: Am. J. Syph., Gonor. & Ven. Dis. **22**:1, 1938.

MATERIAL

This report deals with 112 cases observed during the last three years at the University Hospital and the outpatient department and with the cases of 3 patients treated by one of us (C. M. B.) in private practice.

All age groups from infancy to puberty were affected almost equally. The percentage of Negro patients in this group is approximately the same as in the total number of patients admitted to the institution. The average economic status of the families was poor, and the level of education and of home hygiene was correspondingly low. In most of our cases the patients slept in the same bed with siblings or with the parents. The majority of the mothers were entirely ignorant of the nature of gonorrhea. Vaginal discharge in a child, therefore, usually caused little alarm. Most children were brought to us because of burning on urination or other more serious complications or intercurrent diseases. In at least one sixth of our cases vaginal discharge was discovered on routine examination.

The probable source of infection was known in 33 cases. In 23 cases there was a definite or suggested history of gonorrhea in an adult in the patient's home. A playmate with gonorrhea was found in 2 cases. Two children contracted their infection from sexual intercourse. Four patients were infected in the pediatric ward by a patient with unsuspected gonorrheal vaginitis. Finally, in 2 infants the signs of the vaginal infection were preceded by gonorrheal ophthalmia of the newborn.

DIAGNOSIS

The diagnosis of gonorrhea was established by vaginal smears stained with the Gram stain. If there was any doubt concerning the diagnosis, vaginal cultures were taken by the method of McLeod and his associates.[21] The material for culture was obtained from a cotton-tipped applicator inserted deeply into the vagina. The material was streaked on plates of chocolate agar having a high water content. The plates were incubated at 37 C. in an atmosphere of air reenforced by carbon dioxide. After twenty-four hours the oxidase test with the dye tetramethylparaphenylenediamine hydrochloride was used to detect suspected colonies. Such colonies were examined on gram-stained slides for gram-negative diplococci of typical shape. No fermentation tests were used.

TREATMENT

The administration of theelin (estrone) was started by one of us (C. M. B.) in October 1934 and was used alone or in combination with the vaginal application of 1 per cent silver nitrate jelly until March 1937. (We still use theelin for patients who fail to respond to fever treatment and sulfanilamide.) It was given intramuscularly in oil,[22] 2,000 international units being administered three times weekly. All patients who received theelin as the only form of treatment were treated in the outpatient department unless complications or intercurrent diseases made hospitalization necessary. The vaginal application of 1 per cent silver nitrate jelly was performed in the hospital. Many of the patients did not come regularly for the injections. Minor irregularities of clinical attendance did not seem to interfere with the success of treatment, since our doses were

21. McLeod, J. W.; Coates, J. C.; Happold, F. C.; Priestley, D. P., and Wheatley, B.: J. Path. & Bact. **39**:221, 1934.

22. The theelin in oil of Parke, Davis & Co., was used. Our first 10 or 15 patients were treated with an aqueous solution of theelin. The results were less favorable than with the oily preparation.

well above the minimal effective dose. Determination of the p_H of the vaginal fluid in some of these patients confirmed this point.

Fever was produced by the intravenous injection of typhoid vaccine. The preparation used was a commercial vaccine (Lilly) containing 500,000,000 paratyphoid A bacilli, 500,000,000 paratyphoid B bacilli and 1,000,000,000 typhoid bacilli per cubic centimeter. In our first cases (March through July 1937) not more than one daily injection was given. The initial dose was 0.1 cc. This amount was increased on the next day if the temperature had not risen above 104 F. (40 C.). The dose was further increased if necessary until 1 cc. was reached or a sufficiently high fever was obtained. This procedure did not prove satisfactory because the patients rapidly became resistant to the vaccine and because the period of high fever lasted for only a short time. Later we gave 0.05 to 0.1 cc. of the vaccine intravenously as the initial dose. Subsequent equal or higher doses were given on the same day until temperatures over 104 F (40 C.) were obtained. The patients were wrapped in woolen blankets and covered with a rubber sheet in order to prevent loss of heat by convection and evaporation. Food was withheld and fluids were restricted during the period of fever. Sodium bromide was given before the treatment was started and during the course whenever necessary. Rectal temperatures were taken every ten minutes. The temperature was maintained in most patients on a level between 104 and 106 F. for three to six hours and occasionally longer. The patients were constantly supervised by a special nurse. Most of them stood the treatment well. Chills, vomiting and severe headaches occurred commonly during the first hour after the injection, but in no case did these symptoms necessitate interruption of the treatment. Restlessness was easily controlled by sodium bromide, and headache was relieved by codeine. We did not observe any ill effects resulting from dehydration and loss of chloride. The only more serious complications encountered were hyperthermia (temperature 109 F.) in 1 case and temporary circulatory collapse in another. Both patients recovered spontaneously within thirty minutes. The 2 youngest patients in this group were 8 months old.

Active pulmonary tuberculosis was considered the only contraindication. Roentgenograms of the chest were taken for all children having a positive Mantoux reaction.

Five children were recently treated in the Kettering hypertherm.[23] We believe, as many do, that the production of fever by physical means is superior to the injection of typhoid vaccine. The temperature is more easily controlled, fluids can be given freely, chills do not occur, headaches are rare and the patients do not become refractory to fever-producing agents. We wish to emphasize that we used typhoid vaccine only because of lack of facilities for other methods.

Sulfanilamide was used in the treatment of our patients with vaginitis from July 1937. It was administered orally, 5 grains (0.32 Gm.) per 20 pounds (9.1 Kg.) of body weight being given three times a day for two days, after which 2½ grains (0.16 Gm.) per 20 pounds of body weight was given three times a day for five or more days. The only toxic effect of the drug in this series was a morbilliform rash in 1 patient.

All patients in the last two groups were treated in the hospital.

In addition to the named measures some therapeutic adjuncts were used. These were irrigations with solutions of boric acid or potassium permanganate in a 1:5,000 dilution for patients with a heavy discharge and a "bladder mixture" for patients with urinary complaints. We did not form a separate group for

23. Dr. J. R. Robertson supervised the treatment of these patients.

patients receiving such additional treatment, since these procedures did not seem to influence the course of the disease.

Complications of the vaginal infection were common. We do not know the true incidence of urethral, rectal and cervical gonorrhea in our cases, since we did not take routine smears from the respective regions. Urinary symptoms, such as frequency, dysuria and burning,[24] were complained of by 24 patients. Arthritis was present in 5 cases, and ophthalmia occurred six times. Five patients had definite and 5 others suggested signs of salpingitis and pelvic peritonitis. Five patients had a bloody discharge. This high incidence of complications may be explained by assuming that probably many cases in which no complications occurred did not come under our observation.

FOLLOW-UP PERIOD AND CRITERIA OF CURE

In the earlier part of this study we dismissed our patients after obtaining 3 successive negative smears, usually taken at weekly intervals. During the last six months we did not dismiss any patient before we had at least 1 negative culture and 2 negative smears.

The patients were then allowed to return to school. Reexaminations were made at regular intervals by us in the outpatient department and by the school nurse.

It is known that a long follow-up period is essential if one is to pronounce these patients cured, although there are no generally accepted standards for the length of the period or the number of negative smears required. In this study we tried to compare the results in patients treated one to three years ago with the results in patients treated recently. The follow-up period for the latter group, consisting chiefly of patients treated with fever and sulfanilamide, was relatively short. To overcome this difficulty, we have adopted the term "apparent cures," used previously by several other authors. This term was used, regardless of the final results, in all cases in which 3 or more successive negative smears or cultures were obtained. Several of these patients returned two to twelve months later with a discharge and positive smears. We used the noncommittal term "recurrence" in their cases, since it was impossible to determine accurately whether they had relapses or whether they were reinfected by contacts in the home. It is our impression that reinfections were the most common cause of recurrence.

RESULTS

The results of the treatment with theelin are summarized in tables 1 and 2. Several comments are necessary.

In the group of cases in which there were apparent cures by theelin are included 2 cases in which theelin did not seem to be the deciding factor. In both the patients received an extremely small number of injections. Smears became negative immediately after an intercurrent infection with high fever. In these cases the fever rather than the theelin appears to have effected the cure.

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24. In some cases burning on urination may have been due not to urethritis but to the fact that excoriated areas of the vulva came in contact with the urine during micturition.

In the group under "theelin and fever" smears became negative immediately after the fever therapy in 5 cases; in these cure may be attributed to the fever and in the remaining case to the theelin.

The 22 cases which are excluded from the group under "theelin only, corrected," may be divided into the following subgroups:

1. Those of patients who discontinued treatment after receiving less than fifteen injections (11 cases)
2. Those of patients who received more than 14 injections (11 cases)
   (a) No smears obtained (4 cases)
   (b) One suspected smear only (2 cases)
   (c) One negative smear only (5 cases)

We have excluded these 22 cases, since it does not seem possible to class the patients as either cured or not cured.

TABLE 1.—*Results of Treatment with Theelin*

Treatment	No. of Cases	Apparent Cures		Recurrences	
		Number of Cases	Percentage	Number of Cases	Percentage of Apparent Cures
Theelin (all cases)	82	53	65	7	14
Theelin and 1% silver nitrate jelly	5	5	100	..	..
Theelin and fever	8	7	88	2	29
Theelin only	69	41	59	5	12
Theelin only; insufficient treatment, irregular attendance at clinic, insufficient check-up on smears	22	..	..	..	..
Theelin only, corrected; sufficient treatment, regular attendance at clinic, sufficient check-up on smears	47	41	87	5	12

TABLE 2.—*Dosage of Theelin and Duration of Treatment*

Result	Number of Injections			International Units			Time in Days		
	Minimum	Maximum	Average	Minimum	Maximum	Average	Minimum	Maximum	Average
Apparent cures obtained with theelin (all cases)	6	54	21	12,000	108,000	42,000	12	239	65
First of 3 or more consecutive negative smears or cultures	3	51	18	6,000	102,000	36,000	6	209	54
Apparent cures of acute conditions (less than 2 weeks' duration; 10 cases)	14	51	24	28,000	102,000	48,000	28	239	92
First of 3 or more consecutive negative smears or cultures	10	41	20	20,000	82,000	40,000	14	209	80
Apparent cures of chronic conditions (more than 2 weeks' duration; 16 cases)	6	51	17	12,000	102,000	34,000	12	147	51
First of 3 or more consecutive negative smears or cultures	3	46	15	6,000	92,000	30,000	6	12	42

Twenty-two patients who received theelin two or three years previously were recently reexamined. Seven of these patients had discontinued treatment after receiving doses of theelin which we considered too small to effect a cure or before negative smears were obtained. None of these patients had any treatment in the meantime. Gonorrhea was found in only 1 of these children. Two others had a slight vaginal discharge. Only 2 of these girls had reached puberty. This suggests that spontaneous cure is not an unusual occurrence even before puberty. None of these girls showed any deviation from normal sexual development for their age or any other abnormal condition attributable to the theelin.

The results of the treatment with fever are summarized in table 3. Some patients obtained apparent cures by temperatures much lower than those usually deemed necessary. We did not take vaginal tempera-

TABLE 3.—*Results of Fever Therapy*

Treatment	Number of Cases	Apparent Cures		Recurrence, Number of Cases
		Number of Cases	Percentage	
Fever therapy (all cases)	34	16	47	3
Fever therapy during treatment with theelin	7	6*	86	2
Fever therapy during treatment with sulfanilamide	8	2	25	1
Fever therapy only	19	8	42	..
Temperature over 104 F. for more than 3 hours	22	9	41	1
Temperature over 104 F. for less than 3 hours	12	7†	58	2

* In the remaining case an apparent cure was obtained after continued administration of theelin.

† The temperature of 3 of these patients did not reach 104 F.

tures, nor did we determine in vitro the thermal death time of gonococci from these patients. It is therefore impossible to decide at present whether factors other than the high temperatures contributed to these cures.

In several patients treated with fever slight purulent or mucoid vaginal discharge persisted for several days, in some cases even for many weeks. But repeated smears and cultures were consistently negative.

The results of the treatment with sulfanilamide are summarized in table 4. All 14 patients who responded to sulfanilamide had negative smears within two weeks, 10 of them in less than one week. In case 9 the patient received sulfanilamide for seven days without result. It was discontinued, and two treatments with fever were given. A discharge persisted. A vaginal smear and a culture taken after the fever therapy were positive for gonococci. Administration of sulf-

anilamide was resumed two days later and was continued for two weeks. This time the discharge disappeared rapidly, and smears became negative on the sixth day. We have seen recurrence of discharge or positive smears on discontinuation of the drug, as reported by others,[25] in only 2 cases. In these reinfection could not be excluded. Those patients that were not cured by sulfanilamide did not show any improvement, whereas fever frequently produced marked temporary improvement even if the patient was not cured.

We have made two attempts to improve our results: First, we increased the dose of sulfanilamide to one and one-half or two times

TABLE 4.—*Results of Treatment with Sulfanilamide in Males and Females*

Case No.	Duration of Treatment with Sulfanilamide in Days	Apparent Cure	Day on Which First Negative Smear Was Obtained
	Female Patients		
1	14	—	..
2	7	+	3
3	7	+	4
4	12	+	7
5	7	+	4
6	7	—	..
7	7	+	3
8	9	—	..
9	13 (20)*	+	6 (15)*
10	26	—†	..
11	17	+	3
12	25	—	..
13	16	—†	..
14	28	—†	..
15	32	—†	..
16	33	—†	..
17	35	—†	..
18	37	—	..
19	16	+ recurrence	9
20	9	+	4
21	17	+	5
22	17	+	5
23	5	+‡	3
24	12	+† recurrence	..
25	23	+†	6
	Av. 17.5	Total 14; cures obtained by sulfanilamide alone without recurrence, 10 or 43%	Av. 5.4
	Male Patients		
1 (urethritis)	7	—	..
2 (urethritis)	21	—	..
3 (ophthalmia)	7	—	..
4 (urethritis)	6	+ recurrence	5
4A	20	+†	15

* For explanation see text.
† Fever and sulfanilamide.
‡ Insufficient number of smears.

the previous dose for several patients who were not cured by the smaller dose. None of these patients was further improved or cured. Similarly, prolonged treatment did not cure any patient who did not have negative smears within two weeks. It may have helped, however, to prevent recurrence.

Second, we combined drug therapy with fever treatment. This method was based on the following rationale: Fever therapy causes marked leukocytosis. Domagk,[19] discussing the mode of action of sulfanilamide, stressed the importance of leukocytosis in the treatment of streptococcic infection with this drug. He also cited observations of

25. Crossen.[15] Carey.[17b]

TABLE 5.—*Results of Treatment with Estrogens in Cases Reported Since 1933*

Authors	Number of Cases	Apparent Cures	Percentage	True Cures	Percentage	Recurrences	Percentage of Apparent Cures	Preparation Used	Single Dose*	Duration of Treatment in Days Until Apparent Cure: Range	Duration of Treatment in Days Until Apparent Cure: Average	Total Duration of Treatment in Days: Range	Total Duration of Treatment in Days: Average	Total Dose Given: Range	Total Dose Given: Average
Lewis, 1933 [3b]	8	8	100	6	75	2	25	Aqueous solution of theelin subcutaneously	50-100-200 R.U.	10-98	....	.....	..	850-8,450 R.U.	.....
Lewis and Adler, 1936 [4b].....	33	33	100	25	76	8	24	Theelin suppositories	600-1,000 I.U.	9-48	20.7	.....	..	15,000-50,000 I.U.	27,500 I.U.
Lewis and Adler, 1936 [4b].....	41	35	85	27	66	8	23	Amniotin in ethylene glycol subcutaneously	800 I.U.	14-168	70	.....	..	6,000-83,000 I.U.	28,200 I.U.
Lewis and Adler, 1936 [4b].....	8	8	100	5	63	3	38	Amniotin in ethylene glycol subcutaneously	2,400 I.U.	14-42	24	.....	..	37,000-102,000 I.U.	65,000 I.U.
Witherspoon, J. T.: Am. J. Dis. Child. **50**: 913 (Oct.) 1935	10	0	0	0	0	..	..	Amniotin (Squibb) in ethylene glycol intramuscularly	50-100 R.U. daily	.....	....	42-92	..	Apparently 2,500-5,000 R.U.	.....
Brown, J.: J. A. M. A. **102**: 1293 (April 27) 1934	7	7	100	7	100	..	..	Aqueous solution of theelin (P. D. & Co.)	50-75-100 R.U. daily	Less than 30 days in all cases				400-2,450 R.U.	950 R.U.
Reichert and others, 1937 [27b]	7	6	36	5	71	1	17	Aqueous solution of threelin (P. D. & Co.)	Not stated	Approximately one month				.....	4,228 R.U.
Reichert and others, 1937 [27b]	15	12	80	10	67	2	17	Theelin in oil (P. D. & Co.)	Not stated	Approximately one month				.....	4,228 R.U.
Reichert and others, 1937 [27b]	6	5	83	4	67	1	20	Theelin suppositories (P. D. & Co.)	Not stated	Approximately one month				2,100 R.U.	4,288 R.U.
Reichert and others, 1937 [27b]	10	6	60	4	40	2	33	Placental extracts	Not stated	Approximately one month				.....	4,228 R.U.
Nabarro, S., and Signey, A. G.: Lancet **1**: 604, 1934.....	20	20	100	6	30	14	70	Folliculin menformon by mouth and intramuscularly	Greatly varying	.....	....	26-148	73	6,000-33,000 R.U.	.....
Goldberg, L.; Minier, C., and Smith, E.: J. Pediat. **7**: 401, 1935	16	14	88	14	88	..	..	Amniotin (Squibb) (a) orally; (b) in ethylene glycol intramuscularly	(a) 100-400 R.U. (b) 50-100 R.U.	7-63	39	.....	..	(a) 2,000-23,000 R.U. (b) 900-21,500 R.U. (dose necessary for apparent cure)	Approximately 5,000 R.U.

Miller, 1935 [29]	42	35	83	19	45	16	46	Various substances	Average 50 R.U.	.....	....	.....	..	.....	.....
TeLinde and Brawner, 1935 [27c]	17	17	100	12	71	5	30	Amniotin (Squibb) suppositories	75 R.U.	7-41	17.8	.....	26.3	1,050-4,425 R.U.	1,967 R.U.
TeLinde and Brawner, 1935 [27c]	22	18	82	13	64	5	38	Amniotin (Squibb) in oil subcutaneously	50-1,000 R.U.	7-28	17.5	.....	25.1	1,600-8,250 R.U.	3,600 R.U.
TeLinde and Brawner, 1935 [27c]	16	2	13	2	13	..	..	Amniotin (Squibb) in ethylene glycol; orally, 6; subcutaneously, 10	Orally, 400-2,000 R.U. daily; subcutaneously, 50-100 R.U.	5-116 (2 cases)	61	.....	..	109-191,000 R.U. orally; 400-5,400 R.U. subcutaneously	.....
Limper, M. A., and Hieronymus, E. E.: J. Pediat. **9**: 240, 1936	27	24	89	24	89	..	..	Theelin in oil; theelin in ethylene glycol; estradiol benzoate; folliculin menformon	50-500 R.U.	.....	....	25-115	63	400-10,500 R.U.	4,000 R.U.
Reading, B.: South. M. J. **28**: 464, 1935	8	8	100	8	100	..	..	(a) Theelin, aqueous solution, 2; (b) theelin in oil, 6	(a) 50 R.U. 5 times daily; (b) 300 R.U. 3 times weekly	.....	14	.....	..	1,500-3,800 R.U. until apparent cure; 2,100-6,000, total	.....
Berry, J. V.: Canad. M. A. J. **36**: 396, 1937	25	24	96	17	68	7	30	Theelin	1,000 I.U. 3 times weekly	.....	....	.....	45 56 for acute gonorrhea, 34 for chronic gonorrhea	Not stated	8,000 I.U. for chronic gonorrhea, 1,200 I.U. for acute gonorrhea
Huberman, J., and Israeloff, H. H.: J. A. M. A. **103**: 18 (July 7) 1934	6	6	100	6	100	..	..	Amniotin (Squibb) in ethylene glycol, 5; amniotin orally, 1	Approximately 50 R.U. daily	.....	....	42-63	47	1,800-2,700 R.U., 6,000 orally	2,300 R.U. subcutaneously, 6,000 orally
Sacher, 1937 [27d]	..	Not stated		..	..	..	..	Amniotin (Squibb) suppositories	1,000-2,000 I.U. daily, later twice weekly	.....	....	.....	42	Approximately 27,000-54,000 I.U.	.....
Phillips, R. B.: New England J. Med. **213**: 1026, 1935	13	13	100	4	30	9	70	Theelin in oil (P. D. & Co.)	200-300 R.U. 3 times weekly	28-42	....	28-42	..	2,100-4,460 R.U.	3,160 R.U.
Lewis and Adler, 1937 [17c]....	82	80	97.5	55	67	25	31	Theelin suppositories	1,000 I.U. daily	.....	24	.....	..	.....	.....
Mazer, C., and Israel, S. L.: J. A. M. A. **108**: 163 (Jan. 16) 1937	93	93.2	100.2	75	81	18	81	Estradiol benzoate 500-1,500 R.U. hypodermic	500 R.U. every other day, 1,500 R.U. daily	.....	....	4-8 weeks in most cases 8 weeks	..	8,750-84,000 R.U.	.....

* R.U., rat unit; I.U., international unit; I.R.U., approximately 3 international units.

German clinicians which confirmed this point. We tried the combined treatment in 8 cases. Only 2 patients obtained apparent cures, and one of these had a recurrence.

Recently we had the opportunity to treat two groups of children in whom a single strain of organism was presumably responsible for the infection. The first group consisted of 5 children. Four of these contracted the infection from the remaining child. The other group consisted of 2 sisters who slept together and in whom symptoms of vaginitis developed at the same time. None of the patients in the first group received any benefit from sulfanilamide or from fever therapy. Both patients in the second group had negative smears within five days of treatment with sulfanilamide. Although the number of cases is small, we may take this as suggestive evidence that differences between strains of gonococci rather than differences in the constitution of the patient determine susceptibility to sulfanilamide.

This hypothesis would also explain the fact that patients who once responded to sulfanilamide may be entirely refractory to the drug after contracting a reinfection from a different source.[26]

In our cases, if one of these three methods failed after a fair trial, it was discontinued and another one substituted. A "fair trial" was considered to be fifteen or more injections of theelin, two or more fever treatments with resulting temperatures of over 104 F. for at least four hours or administration of sulfanilamide as described for at least seven consecutive days. Two patients failed to respond to fever but responded to theelin. Three more patients failed to respond to either fever or sulfanilamide and were cured by theelin. Sulfanilamide also failed in 1 girl who was cured by fever. Fever failed in 3 patients who were cured by sulfanilamide. We have had only 1 patient who appeared to be refractory to all three methods.

COMMENT

The literature published since 1933 contains numerous reports on the treatment with estrogens. The results of other authors are briefly summarized in table 5 (only papers written in English are included). It appears from this table, as has been previously stated by others, that theelin or amniotin dissolved in water or in ethylene glycol is inferior to the oily solutions and to vaginal suppositories. The latter are favored by many.[27] The majority of authors obtained results

26. Robertson, J. R.: Personal communication to the authors.

27. (*a*) Lewis and Adler.[4b] (*b*) Reichert, J. L.; Epstein, I. M.; Jung, R., and Colwell, C. A.: Infection of the Lower Part of the Genital Tract in Girls, Am. J. Dis. Child. **54**:459 (Sept.) 1937. (*c*) TeLinde, R. W., and Brawner, J. N.: Am. J. Obst. & Gynec. **30**:512, 1935. (*d*) Sacher, C. B.: Texas State J. Med. **32**:809, 1937.

comparable with ours, with 80 to 100 per cent apparent cures. These were obtained on the average within twenty to fifty days. Acute gonorrhea required longer treatment than a chronic condition. Regularity and duration of treatment appeared to be more important than the amount given in a single or total dose. Increase of the minimal effective dose did not seem to improve the results. An average of 15 to 30 per cent of the apparently cured patients showed recurrences. In most of the cases a relapse responded to another course of theelin. In few cases did the condition appear to be refractory.

There is still some uncertainty about the possible dangers of the treatment. These are stated to be (1) development of secondary sexual characteristics; (2) a deleterious effect on the ovary, and (3) development of the upper genital tract, aiding the spread of the gonococcic infection to the tubes and ovaries.

We have noticed enlargement of the breasts, slight growth of pubic hair and occasional spotting in a few of our cases. All these signs disappeared soon after the discontinuation of the treatment. This is in accord with the observations of all other authors. The effects on the ovary have been investigated by numerous authors, the majority of whom agree that estrogens are relatively innocuous if administered in the usual therapeutic doses over a limited period of time.

One of our patients died of heart disease two months after discontinuation of the theelin. This patient had received 40,000 international units over a period of forty days. At autopsy no deviation from the normal was observed macroscopically or microscopically in the genital tract, including the ovaries, or in any of the endocrine glands.[28] Miller [29] also reported the normal histologic appearance of ovarian tissue removed for biopsy from one of his patients.

In 1 patient gonococcic salpingitis developed during the treatment with theelin. The treatment was not discontinued, and the patient recovered. We were unable to find in the literature any reports describing the development of pelvic infection during treatment with theelin. It therefore seems impossible to prove a causal relationship between the theelin therapy and the development of salpingitis in our case.

The final results of the treatment with theelin were better than those obtained by the two other methods. The good results obtained in adults by fever therapy with proper equipment are suggestive evidence that the results in gonorrheal vaginitis could be considerably improved. A good percentage of the cases could be cured within a short time. The cost of hospitalization and the period of contagiousness

28. Dr. E. Pund, of the Department of Pathology, examined these organs and interpreted the findings.

29. Miller, J. R.: Am. J. Obst. & Gynec. **29**:553, 1935.

were markedly reduced. The rapidity of the cures was also an outstanding feature of the treatment with sulfanilamide. We know little about the frequency of recurrences after these two forms of treatment. However, it can be expected that there will be fewer true relapses. The relapses occurring in patients treated with theelin are generally attributed to reinfection from foci in the urethra or in the rectum. Fever and sulfanilamide presumably affect the gonococci in all tissues equally. Complications are therefore likely to be equally benefited.

Both methods are still in the experimental stage. We do not recommend them for routine use in general practice or for ambulatory patients. But we hope that they will be tried on a large scale in other institutions. The preliminary results appear promising.

SUMMARY AND CONCLUSIONS

One hundred and twelve cases of gonorrheal vaginitis were under our observation during the last three years. In most of the cases the infection was probably acquired from an adult in the patient's home. Complications were common in our series.

Apparent cures following the intramuscular injection of theelin in oil as the only form of treatment were obtained in 41 of 47 cases (87 per cent). In 5 of these (12 per cent) there were recurrences. Five patients treated with theelin and 1 per cent silver nitrate jelly were cured and did not have recurrences.

Apparent cures following fever as the only method of treatment were obtained in 8 of 19 cases (42 per cent). There was 1 recurrence (12.5 per cent). In 6 of 7 patients treated with fever during theelin therapy apparent cures could be attributed to the fever. The fever was produced by the intravenous injection of typhoid vaccine and in 5 cases by the Kettering hypertherm.

Apparent cures followed the oral administration of sulfanilamide as the only method of treatment in 11 of 22 cases (50 per cent). One patient had a recurrence. Two patients were cured by a combined treatment with fever and with sulfanilamide. One of these had a recurrence.

All cures due to sulfanilamide were obtained in less than two weeks. Increase of the dose, prolongation of the treatment and combination with fever therapy did not improve the results.

The literature on the treatment of vaginitis with estrogenic substances is briefly reviewed.

Fever therapy and treatment with sulfanilamide are recommended for further investigation. Possible advantages of their use are discussed.

Social work done by Mrs. E. Lester made possible the completion of this study.

CIRCULATORY FUNCTION IN THE ANEMIAS OF CHILDREN

I. EFFECT OF ANEMIA ON EXERCISE TOLERANCE AND VITAL CAPACITY

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In the later years of the nineteenth century, several writers on chlorosis described the occurrence of cardiac murmurs and enlargement of the heart and the postmortem observation of myocardial dilatation, hypertrophy and degeneration.[1] Since that time similar changes have been noted with many varieties of anemia, especially with the more chronic forms, such as the pernicious, the sickle cell and the erythroblastic type. Other symptoms and signs have been described, and the pathology of the cardiovascular system has been more carefully studied.[2]

Dr. Parsons' work was done during the tenure of the Walter Myers Traveling Studentship.

From the Babies Hospital and the Department of Diseases of Children, Columbia University.

1. Irvine, P.: On the Clinical Condition of the Heart and Vessels in Chlorosis, Lancet **1**:837, 1877. Barrs, A. G.: Clinical Observations on the Cardiac Bruits of Chlorosis, Am. J. M. Sc. **102**:347, 1891. Hersman, C. F.: Temporary Mitral Insufficiency in Anemic Conditions, Internat. M. Mag. **2**:341, 1893. Gautier, E.: Ueber die morphologischen Veränderungen des Herzens bei der Chlorose auf Grund klinischer Beobachtungen, Deutsches Arch. f. klin. Med. **62**:120, 1899.

2. (*a*) Goldstein, B., and Boas, E. P.: Functional Diastolic Murmurs and Cardiac Enlargement in Severe Anemias, Arch. Int. Med. **39**:226 (Feb.) 1927. (*b*) Bouchut, L., and Froment, R.: Les gros coeurs par anoxémie à propos des anémies pernicieuses, compliquées d'hypertrophie et d'insuffisance cardiaques, Arch. d. mal. du cœur **27**:325, 1934. (*c*) Strieck, F.: Zur Symptomatologie der Biermerschen Krankheit, Med. Klin. **20**:1538, 1924. (*d*) Wallgren, A.: Die Arterien der Niere und der Blutdruck, Acta med. Scandinav. **56**:356, 1922. (*e*) Cabot, R. C.: Facts on the Heart, Philadelphia, W. B. Saunders Company, 1926. (*f*) Yater, W. M., and Hansmann, G. H.: Sickle-Cell Anemia: New Cause of Cor Pulmonale, Am. J. M. Sc. **191**:474, 1936. (*g*) Nemet, G., and Gross, H.: Cardiac Hypertrophy in a Case of Cooley's Anemia, Am. Heart J. **12**:352, 1936. (*h*) Manne, A. S., and Kuskin, L.: Acute Hemolytic Anemia in Childhood with Unusual Cardiac Manifestation, J. Pediat. **4**:789, 1934. (*i*) Ball, D.: Changes in the Size of the Heart in Severe Anemia, Am. Heart J. **6**:517, 1931. (*j*) Kraus,

(Footnote continued on next page)

Anemia may produce signs which suggest primary heart disease. The murmurs are not necessarily of the so-called hemic type, in which the bruit is systolic in time and is confined to the base of the heart, but they may be heard in both systole and diastole and may be either generalized or localized to any of the valvular areas.[3] In young patients such murmurs are often transmitted to the axilla and even to the back. A low diastolic pressure which causes the pulse to assume a water hammer character may make the simulation of valvular disease even more complete.[4] With certain anemias, notably sickle cell anemia, pains in the bones or joints, pyrexia and an abnormally high erythrocyte sedimentation rate are sometimes present and may make it difficult to distinguish the condition from rheumatic fever.[5] From such beginnings the picture may progress to one of cardiac failure, with venous congestion, edema, enlargement of the liver and dyspnea.[6] In other cases angina pectoris may supervene.[7] For the most part, published studies of the cardiac complications of anemia have been concerned with adults and have been limited to a presentation of the clinical syndromes involved; there have been few descriptions of similar findings in children and few investigations of the functional capacity of the heart in such patients.

The most important consequence of anemia is reduction in the oxygen-carrying capacity of the blood. Since the oxygen requirement of the various tissues remains approximately the same whether or not anemia is present, compensatory mechanisms are brought into play in order to ensure that the tissues receive sufficient oxygen. Such adjustments are of several kinds. For example, it has been demonstrated that the tissues extract a larger percentage of the oxygen from anemic blood as it passes through the capillaries, satisfying their oxygen needs at the expense of the venous blood, which is returned to the heart greatly

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F.: Die klinische Bedeutung der fettigen Degeneration des Herzmuskels schwer anämischer Individuen, Berl. klin. Wchnschr. **42**:111, 1905. (*k*) Anderson, W. W., and Ware, R. L.: Sickle Cell Anemia, Am. J. Dis. Child. **44**:1055 (Nov.) 1932.

3. Friedreich, N., in Virchow, R.: Handbuch der speciellen Pathologie und Therapie, Erlangen, Ferdinand Enke, 1861, vol. 2, p. 227. von Noorden, C.: Untersuchungen über schwere Anämien, Charité-Ann. **16**:217, 1891. Sahli, H.: Ueber diastolische accidentelle Herzgeräusche, Cor.-Bl. f. schweiz. Aerzte **25**: 33, 1895. Goldstein and Boas.[2a] Manne and Kuskin.[2h]

4. Morse, J. L.: Functional Diastolic Murmurs in the Aortic Area, and Pistol Shot Sounds in the Groins in Infancy and Childhood, Arch. Pediat. **41**:559, 1924.

5. Yater and Hansmann.[2f]

6. Bartels, E. C.: Anemia as a Cause of Severe Congestive Heart Failure, Ann. Int. Med. **11**:400, 1937.

7. Stalker, H.: Angina Pectoris and Pernicious Anemia: Résumé of the Literature with a Case Report, Ann. Int. Med. **10**:1172, 1937.

depleted of this element.[8] It has also been shown that the amount of blood circulated during each minute is increased; the minute volume of the heart is greater, owing in part to a faster cardiac rate and in part to a larger stroke volume,[9] while at the same time the rate of circulation is more rapid.[10]

The cardiovascular system thus compensates for anemia by bringing blood more quickly to the tissues. Although the amount of oxygen carried by each cubic centimeter of blood is small, the total volume supplied to the tissues in each minute is thereby rendered adequate for their needs. It is apparent, therefore, that the heart and vessels are of supreme importance to the anemic patient and that if they fail he may be completely crippled. Such a risk of failure is by no means remote, for in addition to the strain of constant overwork the heart is embarrassed by a continual deficiency of properly oxygenated blood. It is therefore important to investigate cardiovascular function in cases of anemia in order to determine how severely the heart is damaged and whether the injury is remediable in whole or in part. For such a study the anemias of children are ideal, since there are no complicating factors such as sclerosis of the coronary arteries, which frequently plays so important a part in the production of myocardial disease in adults.

The heart and circulation may be studied in a variety of ways. Probably the methods most commonly used for investigating cardiac function are the estimation of exercise tolerance and the measurement of the vital capacity of the lungs. These two forms of examination have been employed frequently in studies of heart disease, both in adults and in children; if there is any limitation of the cardiac reserves, the tests usually show some abnormality. In some cases damage to the heart can be most readily identified by electrocardiographic examination. As the heart fails the venous pressure rises, and the right side of the heart may

8. (*a*) Lundsgaard, C.: Studies of Oxygen in Venous Blood, J. Exper. Med. **30**:147, 1919. (*b*) Harrop, G. A.: Oxygen and Carbon Dioxide Content of Arterial and Venous Blood in Normal Individuals and in Patients with Anemia and Heart Disease, ibid. **30**:241, 1919. (*c*) Liljestrand, G., and Stenström, N.: Work of the Heart During Rest: Influence of Variations in Hemoglobin Content on Blood Flow, Acta med. Scandinav. **63**:130, 1925. (*d*) Nielsen, H. E.: Circulation in Anemic Condition, ibid. **81**:571, 1934.

9. Fahr, G. E., and Ronzone, E.: Circulatory Compensation for Deficient Oxygen Carrying Capacity of the Blood in Severe Anemias, Arch. Int. Med. **29**: 331 (March) 1922. Grollman, A.: The Cardiac Output of Man in Health and Disease, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

10. Seckel, H.: Blood Volume and Circulation Time in Children, Arch. Dis. Childhood **11**:21, 1936. Blumgart, H. L.; Gargill, S. L., and Gilligan, D. R.: Studies on Velocity of Blood Flow: Velocity of Blood Flow and Other Aspects of the Circulation in Patients with Anemia, J. Clin. Investigation **9**:679, 1931. Liljestrand and Stenström.[8c]

become dilated as the venous engorgement increases. Changes in cardiac size are not easily measured clinically but may be followed with considerable accuracy by roentgen study.

We therefore decided to study the hearts of a group of anemic children during the course of their disease, before and after treatment had been given, watching the effect of therapy on exercise tolerance, vital capacity, venous pressure, electrocardiograms and roentgen measurements of the heart. Furthermore, in order to confirm observations of other investigators, it was necessary to measure the oxygen saturation of arterial and venous blood, to determine the circulatory rate and to calculate the output of the heart. By these means we hoped to throw further light on the way in which the cardiovascular reserves are affected by chronic anemia and to determine whether any changes which have occurred are permanent or are capable of recovery.

In the following report are résumés of the clinical histories of the 5 anemic children who served as subjects for all of the investigations just cited.

REPORT OF CASES

CASE 1.—S. R., a Jewish boy of 7 years, was admitted to the Babies Hospital for the thirty-seventh time when these studies were made. His numerous admissions were necessitated by the presence of an aregenerative type of anemia which selectively affected the red blood cells. At the time of study he had received sixty-six transfusions given at intervals of one to three months since early infancy.

The child was born on May 28, 1930, after a difficult delivery. Until his first visit to the Babies Hospital, at the age of 3 months, he seemed to be normal in every respect. Pallor was first noted at this time, and one month later examination of the blood revealed a hemoglobin concentration of 20 per cent, 970,000 red blood cells per cubic millimeter, no reticulocytes and a normal total leukocyte count and differential count except for slight eosinophilia. The first transfusion was administered at this time.

During the first two years of life the child suffered repeated infections of the upper respiratory tract. Although the appetite was only fair, he consumed adequate amounts of solid food and vitamins. Numerous forms of therapy were tried in an attempt to stimulate the production of red blood cells by the bone marrow. From the age of 4 months the boy continually received some form of iron or liver or both. In addition, a combination of liver and stomach extract and iron (lextron), liver extract-Lilly (intramuscularly), copper, ascorbic acid (intravenously), desiccated hog stomach, gastron and beefsteak followed by normal human gastric juice were administered for varying periods. Of these medicaments, only the intramuscularly injected liver extract-Lilly produced any reticulocytosis, and then the response was sustained for four days only. Hundreds of preparations of blood were examined for the presence of reticulocytes, but only five or six showed any such cells, and their number never exceeded a fraction of 1 per cent. Because of this nearly complete lack of erythropoiesis, the patient was forced to return to the hospital for transfusion whenever the hemoglobin concentration fell to 15 or 20 per cent. The interval between transfusions was variable, being generally about six to ten weeks.

The child's clinical appearance was characterized by pallor of the skin and mucous membranes with light lemon yellow pigmentation but no jaundice. During the later admission a green tinge of the skin and gray cyanosis of the lips were described. At times, when the hemoglobin concentration was low, there were dyspnea on slight exertion, anorexia, fatigability and slow speech and reactions, with distinct mental torpor. Immediately after transfusion the patient's activity increased, and he became fairly alert mentally. On one occasion his intelligence quotient was rated as low average. His gait was always spastic and slightly ataxic, but neurologic examination never revealed loss of sensation for position or vibration, and the presence of pathologic changes in the posterolateral columns could not be established. Throughout the period of observation the liver enlarged very slowly; the spleen, though palpable at times, was never greatly enlarged.

No cardiac abnormalities except tachycardia were noted until the end of the first year, when a faint systolic murmur first became audible. This gradually increased in intensity and in area of transmission until it became a constant finding during periods of anemia, fading again after transfusion. Clinical evidence of cardiac enlargement was variable, but on two occasions roentgen examination of the chest demonstrated a definite but slight increase in the transverse diameter of the heart. The blood pressure was always within normal limits. Edema and signs of pulmonary congestion were not encountered. No circulatory embarrassment followed transfusion, but transient febrile responses were not infrequent.

The significant blood values recorded during the period of study were as follows:

	Before Transfusion	After Transfusion
Red cells in millions per cubic millimeter	1.54	2.61
Oxygen capacity in volumes per cent	5.67	11.20
Hemoglobin content calculated from oxygen capacity, expressed in grams per hundred cubic centimeters	4.59	9.07

The boy received two transfusions, of 250 and 300 cc. respectively, with a twenty-four hour interval between. The weight was 21.6 Kg. and the height 114 cm.

Case 2.—M. M., an Italian girl of 7½ years, had been making regular visits to the Babies Hospital since the age of 8 months because of erythroblastic anemia. At the time of our investigation she was admitted for the thirty-fourth time, in order to receive her forty-seventh transfusion. Both her parents were born in Italy. An older brother was well. The child's birth was normal, and she seemed well until the age of 4 months, when her mother noticed that she was pale and brought her to the hospital. Physical examination disclosed the typical picture of Cooley's anemia: Italian race, marked pallor, dark skin and extremely large liver and spleen. Examination of the blood confirmed the clinical impression, revealing normocytic anemia, reticulocytosis, normal leukocytes and large numbers of normoblasts and megaloblasts in the smear.

In spite of continuous administration of liver and iron, the red blood cell count and the hemoglobin concentration fell persistently, which necessitated transfusion every two or three months. Evidence of hemolysis was slight; there was never any jaundice, and the fragility of the red cells was normal. Because of abdominal discomfort, splenectomy was performed at the age of 22 months. This was followed by a marked increase in the number of platelets and erythroblasts in the circulating blood. The mongoloid features characteristic of the disease developed as the patient grew. Pari passu, roentgen study of the skull and of the long bones showed the evolution of widened marrow spaces, irregular trabeculation, thinning of the cortices and squaring of the ends of the bones.

At the age of 1 year a systolic cardiac murmur was noted for the first time. This gradually increased in intensity and in area of transmission and became a constant finding in later physical examinations. From the second year on, progressive enlargement of the heart was also noted both by clinical and roentgen study. During the periods of low hemoglobin concentration, tachycardia and dyspnea were present on slight exertion. The blood pressure remained normal. The liver was invariably enlarged. On four occasions pretibial edema associated with normal values of serum protein was present before transfusion.

The interval between transfusions varied from one to four months. At each admission blood was given in amounts which ranged from 300 to 800 cc., the dose being generally divided and given on consecutive days. The procedure was frequently followed by brief but high fever, but never by signs of embarrassment of the heart.

When admitted for these investigations the patient was exceedingly anemic and in a state of mild cardiac decompensation. The height was 118.5 cm., the weight 25.3 Kg., the temperature 100.2 F., the pulse rate 112, the respiratory rate 22 and the blood pressure 92 systolic and 56 diastolic. The child was dull, apathetic, dyspneic and orthopneic, with pronounced grayish pallor and pitting edema of the lower extremities. The heart was greatly enlarged to the left on percussion, and a harsh systolic murmur was audible all over the precordium and in the back. The lungs were free of rales; the liver extended to the iliac crest and was firm but not tender. The venous pressure was elevated and the circulation time prolonged. After three days' rest in bed there was diminution in peripheral edema, and the respirations became easier, but the other findings were not changed. The first series of determinations was made at this time.

Four transfusions (1,150 cc. being given in all) were administered during a period of five rays. The hemoglobin concentration increased from 14 to 85 per cent (Sahli), and the red blood cell count rose from 1,240,000 to 3,830,000. After the last transfusion the girl seemed vaguely uncomfortable and vomited several times, and on the following day bradycardia (60 per minute) and hypertension (138 systolic and 104 diastolic) were observed. In certain respects the child seemed improved: the dyspnea was gone, the liver smaller and the venous pressure normal.

Three days after the last transfusion the patient lapsed into coma; she recovered half an hour later, but twelve hours later she reverted to the unconscious state. Hypertension was then pronounced, and violent generalized convulsions set in. The child became dyspneic and cyanotic and appeared moribund. Sedatives were given, magnesium sulfate was administered intramuscularly and phlebotomy was performed. The girl improved slowly during the next four weeks, but uncertain gait, moderate motor aphasia and general depression of the cerebral functions remained. Although a lumbar puncture yielded normal spinal fluid, it was felt that the patient had suffered thrombosis of a cerebral vessel and acute cerebral edema. Because of this unfortunate reaction we were forced to postpone the second series of determinations until five weeks after the last transfusion. At this time the following blood values (in the second column) were obtained:

	Before Transfusion	After Transfusion
Red cells in millions per cubic millimeter	1.24	2.60
Oxygen capacity in volumes per cent	3.62	8.60
Hemoglobin content calculated from oxygen capacity, expressed in grams per hundred cubic centimeters	2.94	5.35

Blood was administered in doses of 150, 250, 250, 275 and 225 cc. The last two transfusions were given on the same day but twelve hours apart.

CASE 3.—G. G., a 7 year old Italian girl, was observed sporadically at the Babies Hospital from infancy. Both the parents were born in Italy. An older brother was in good health. The child's birth was normal; her progress was complicated by otitis media at the age of 4 months. At 5 months the patient was admitted to the hospital because of diarrhea. The physical examination at this time disclosed marked pallor, enlargement of the liver and of the spleen and otitis media. The heart was rapid, with poor sounds but no murmur. Examination of the blood showed a hemoglobin concentration of 40 per cent (Sahli) and a red blood cell count of 2,550,000 per cubic millimeter, with 0.16 per cent reticulocytes, normal leukocytes and a moderate number of normoblasts in the smear. The van den Bergh reaction of the blood serum was faintly positive to the indirect test; 1.8 mg. of urobilin was excreted in the urine in twenty-four hours. The Kahn reaction and roentgenograms of the long bones were normal.

The exact nature of the anemia did not become apparent until the age of 8 months, when the blood smear showed large numbers of erythroblasts and megaloblasts, suggestively mongoloid features were noted and the roentgenograms of the skull and of the long bones showed the first definite evidence of erythroblastic anemia. On June 2, 1931, splenectomy was performed, following which there were a moderate increase in the number of erythroblasts in the circulating blood and a marked increase in platelets. Pathologic study of a section of the spleen confirmed the diagnosis. Subsequently typical mongoloid features appeared, and advanced changes in the bones were discovered by roentgen examination.

Owing to an unusual lack of interest on the part of the parents, who flatly refused to donate blood and who were extremely remiss in keeping clinical appointments, medical supervision of the patient was poor and therapy minimal. On one occasion the child escaped medical surveillance for as long as three and one-half years. Except for brief periods following the five transfusions which she received, she lived with a hemoglobin concentration ranging between 20 and 40 per cent for the first seven years of her life. Treatment was limited to these sporadic transfusions and to irregular administration of liver and iron.

At the age of 5 months no definite cardiac abnormalities were discovered other than tachycardia. At 9 months a systolic murmur was first heard, and a roentgenogram of the chest showed slight but definite enlargement of the cardiac silhouette. At 5 years the clinical evidence of cardiac abnormality was unmistakable. The cardiac borders were wide on percussion; the heart sounds were rapid and forceful, with a loud systolic murmur all over the precordium, and the roentgenographic cardiothoracic index was 0.77.

The patient was always weak and tired. The appetite was poor. The girl was plagued by repeated infections of the upper respiratory tract. Her growth did not keep pace with that of other children of like age, but despite the fact that she never attended school she was bright and alert. Signs attributable to congestive heart failure were never in evidence.

At the time of our studies the patient was admitted for the seventh time and received her sixth transfusion. The temperature was 99.8 F., the pulse rate 100, the respiratory rate 22 and the blood pressure 92 systolic and 52 diastolic. The features were mongoloid, and the skin was a dark olive color. The tonsils were large and chronically infected. The girl was slightly dyspneic but was able to be up and about the ward. The lungs were clear. The liver extended 4 cm. below the costal margin; peripheral edema was absent. The cardiac findings have been described.

The significant blood values follow:

	Before Transfusion	After Transfusion
Red cells in millions per cubic millimeter	1.9	2.3
Oxygen capacity in volumes per cent	6.17	8.24
Hemoglobin content calculated from oxygen capacity, expressed in grams per hundred cubic centimeters	5.00	6.66

The child received two transfusions, 150 cc. being given each time, with an interval of twenty-four hours between. The weight was 18 Kg.

CASE 4.—R. R. was an Italian boy of 4 years suffering from erythroblastic anemia. He was born in Sloane Hospital on Aug. 30, 1933, about one month prematurely. The weight at birth was 2,060 Gm. The first year of life was complicated only by minor difficulties in feeding, and not until the child passed his first birthday was the presence of chronic anemia suspected. Pallor and enlargement of the liver and spleen led at this time to an investigation of the blood, which revealed many (8,600 per cubic millimeter) nucleated red blood cells in the smear. The subsequent clinical course confirmed the diagnosis of erythroblastic anemia, since the patient acquired mild icterus, mongoloid features and roentgen changes in the long bones typical of the disease.

Between the first and third years of life the boy was admitted to the hospital for transfusion at least every two months. On admission the hemoglobin concentration generally ranged around 35 per cent; it was increased to about 75 per cent after injections of blood in amounts varying from 150 to 600 cc. During this period the spleen enlarged progressively, and on Sept. 28, 1936, it was removed for symptomatic relief. Microscopic sections of this organ confirmed the original diagnosis. During the year preceding this study, the rate of hemolysis diminished so that only three transfusions were required, bringing the total up to eighteen.

Clinical evidence of derangement of cardiac function fluctuated with the level of the hemoglobin concentration. Before transfusions pallor, tachycardia and a systolic murmur at the apex of the heart were generally present. Enlargement of the heart was not consistently demonstrated by percussion and could not be confirmed by roentgen examination. Cyanosis, edema, hypertension and evidence of pulmonary congestion were never observed. During the period of observation there was a slow but progressive increase in the size of the liver. The child was alert, active and intelligent.

The significant blood values follow:

	Before Transfusion	After Transfusion
Red cells in millions per cubic millimeter	2.80	4.58
Oxygen capacity in volumes per cent	10.07	14.19
Hemoglobin content calculated from oxygen capacity, expressed in grams per hundred cubic centimeters	8.14	11.49

The weight was 14.5 Kg. and the height 86 cm. The patient received two transfusions, 300 cc. being given each time, with an interval of two days between.

CASE 5.—J. S. was a Jewish girl of 6 years who was admitted to the Babies Hospital on Oct. 4, 1937, for tonsillectomy. Previously her health had always been good except for repeated attacks of sore throat during the winter months.

The child never suffered any rheumatic symptoms. On October 5 tonsillectomy and adenoidectomy were performed, at which time a complete physical examination disclosed nothing unusual other than chronic infection of the lymphoid tissues of the pharynx. On October 12 the girl returned to the hospital because of protracted bleeding from the nose. A large clot was removed from the nasopharynx, and the hemorrhage ceased. At this time the physical examination revealed pallor of the skin and of the mucous membranes, rapid pulse and a heart which was normal in size and without murmurs. The blood pressure was 120 systolic and 68 diastolic.

The significant blood values were as follows:

	Before Transfusion	After Transfusion
Red cells in millions per cubic millimeter	2.1	3.4
Oxygen capacity in volumes per cent	8.21	13.08
Hemoglobin content calculated from oxygen capacity, expressed in grams per hundred cubic centicentimeters	6.65	10.58

The patient received 300 cc. of blood by a single transfusion. The weight was 20.1 Kg. and the height 114 cm.

TABLE 1.—*Blood Values of Anemic Patients Before and After Treatment* *

Case No.	Type of Anemia	Age, Yr.	Weight, Kg.	Oxygen Capacity, Vol. per Cent	Red Cell Count, Millions	Transfusion, Cc.
1	Aplastic	7	21.6	5.67 11.20	1.54 2.61	550
2	Erythroblastic	7	25.3	3.62 8.60	1.24 2.60	850 (?)
3	Erythroblastic	7	18.0	6.17 8.24	1.90 2.30	300
4	Erythroblastic	4	14.5	10.07 14.19	2.80 4.58	600
5	Secondary	6	20.1	8.21 13.08	2.10 3.40	300

* In this and in succeeding tables, in all cases in which 2 values are given for a test the first indicates the result before treatment and the second the result after treatment.

The blood counts of the children before and after treatment are set out in table 1. It will be noticed that the rise in red cells and in hemoglobin content which followed therapy was not remarkable. The figures, however, are representative of the improvement which is expected when a patient with chronic anemia pays his periodic visit to the hospital for transfusion. This matter is important and will be discussed more fully in a later paper.

METHODS OF STUDY

There is no standard technic for the estimation of exercise tolerance, but all the methods are the same in general principle. In the present instance the pulse rate (counted by auscultation over the precordium), blood pressure (measured by means of a mercury sphygmomanometer) and respiratory rate were noted while the child was at rest. Three flights of stairs were then climbed in approximately forty seconds, and similar readings were made immediately and at the

end of each minute for five minutes. If the heart is normal the various measurements should return to the resting level, or at least to within 2 to 5 points of this level, by the end of the second minute after the completion of exercise.[11]

Vital capacities were measured with a Krogh spirometer, the best of several readings being recorded.

Control observations were made on 10 children of similar age whose blood values and circulatory systems were normal.

RESULTS

The results of the various procedures are given in tables 2 to 5. The figures in parentheses represent the point at which the resting values were regained. A deviation of 5 points was allowed for the pulse rate and the respiratory rate and of 10 for the blood pressure.

TABLE 2.—*Effect of Exercise on Pulse Rate Before and After Treatment*

Case No.	At Rest	1st Minute	2d Minute	3d Minute	4th Minute	5th Minute
			Anemic Subjects			
1	110	122	(105)	100	96	102
	96	116	106	(80)	88	90
2	120	132	126	(112)	112	120
	84	99	(74)	75	78	80
3	108	141	116	(108)	104	108
	92	123	(82)	90	88	90
4	120	(125)	112	108	114	116
	80	96	(82)	84	86	84
5	120	152	132	(120)	122	120
	120	138	130	(120)	116	120
			Control Subjects			
6	64	88	(58)	66	66	
7	80	100	(66)	78		
8	72	144	80	(60)		
9	72	80	(75)	78	72	76
10	66	(70)	63	70	66	70
11	72	80	(72)	72	72	72
12	96	(96)	104	104	100	102
13	132	140	(128)	136	136	132
14	66	84	(64)	66	68	68
15	80	96	(84)	82	90	82

Pulse Rate.—From table 2 it will be seen that exercise tolerance as estimated by the pulse rate was not grossly abnormal. At the end of the second minute the pulse rates of 2 of the children with chronic anemia (cases 1 and 4) had fallen to the resting level. The tolerance of the other 2 patients with long-standing anemia (cases 2 and 3) barely fell outside the normal limits. The child with acute anemia (case 5) reacted in a more abnormal manner, since at the end of the second minute her pulse rate was still above the resting level by 12 beats. All but 1 of the control subjects regained the preexercise figure in two minutes. The resting pulse rates of the anemic children were distinctly higher than all save 1 of the controls.

11. Schmitz, H. W.: Vital Capacity, Respiratory Frequency, Pulse Rate, and Systolic Blood Pressure in Heart Disease: Their Importance in the Classification of Patients, Arch. Int. Med. **36**:628 (Nov.) 1925.

After transfusion the resting pulse became slower in those children with chronic anemia but was not altered in the child with an acute condition. The tolerance for exercise was better in 3 of the 4 children with chronic involvement and unchanged in the child with acute disease.

Respiratory Rate.—The figures in table 3 show that by the end of the second minute all the controls and the 4 anemic patients whose anemia was of long standing were breathing at the resting rate again. Values obtained for the child with acute anemia fell distinctly outside the normal range, and her response was no better after treatment. Transfusion produced a pronounced drop in the resting respiratory rate in case 2.

Blood Pressure.—Fluctuations in the level of systolic blood pressure during the five minutes following exercise were greater than expected, but they were present in both anemic and control subjects. In table 4 it is seen that the systolic pressure of 4 of the control subjects failed to return to the resting level before the third minute. One patient with chronic anemia (case 1) showed a similar abnormality, with slight improvement after transfusion. The patient with acute anemia (case 5) also had a poor response but reacted normally after transfusion.

Measurements of diastolic blood pressure showed less fluctuation. As a rule the diastolic pressure fell immediately after exercise, when the systolic pressure was at its height. Diastolic pressures during rest were usually higher after treatment.

Vital Capacity.—The vital capacities of the anemic children were considerably less than those of the normal controls, even when computed in relation to height. The 3 children with erythroblastic anemia showed an increase in vital capacity after transfusion, but their values failed to approach the normal range.

COMMENT

One of the remarkable features about children suffering from severe but chronic forms of anemia is the absence of apparent restriction of their ability to take exercise. We have repeatedly noticed that children with a red blood cell count of 2,000,000 or less may play with all the vigor of their healthy brothers and sisters and yet fail to display dyspnea or other symptoms of embarrassment. It would appear that in some way these patients succeed in becoming adapted to their abnormal internal environment. Our clinical observations agree with the view that it is a feeling of lassitude and of weakness of the limbs, rather than shortness of breath, which eventually limits activity.[12] This suggests

12. (*a*) Peabody, F. W., and Wentworth, J. A.: Clinical Studies of the Respiration: IV. The Vital Capacity of the Lungs and Its Relation to Dyspnea, Arch. Int. Med. **20**:443 (Sept.) 1917. (*b*) Lambie, C. G.: The Functional Pathology of Anaemia: Symptoms and Signs of Anaemia, M. J. Australia **2**:423, 1937.

that, as in normal subjects, it is the skeletal muscle rather than the myocardium which first fails to respond to an increased amount of

TABLE 3.—*Effect of Exercise on Respiratory Rate Before and After Treatment*

Case No.	At Rest	1st Minute	2d Minute	3d Minute	4th Minute	5th Minute
			Anemic Subjects			
1	24	36	(24)	30	28	22
	26	32	(28)	24	20	24
2	40	56	(44)	36	32	32
	30	40	(30)	28	..	28
3	32	38	(24)	22	28	28
	30	(32)	32	30	30	28
4	36	(32)	36	32	36	32
	32	44	(36)	40	36	36
5	30	48	38	36	(28)	32
	32	44	40	40	(32)	36
			Control Subjects			
6	26	36	(28)	24	24	..
7	30	(32)	32	28	26	..
8	..	..	..	..	..	..
9	30	36	(32)	28	28	32
10	24	(28)	28	24	24	20
11	28	36	(30)	32	32	24
12	22	(24)	20	22	22	16
13	22	32	30	32	32	28
14	28	(26)	26	26	20	26
15	26	(28)	26	..	..	..

TABLE 4.—*Effect of Exercise on Systolic Blood Pressure Before and After Treatment*

Case No.	At Rest	1st Minute	2d Minute	3d Minute	4th Minute	5th Minute
			Anemic Subjects			
1	110	145	135	125	(118)	116
	110	135	125	(120)	110	110
2	104	(110)	106	114	110	110
	115	(120)	120	120	...	106
3	100	120	(108)	105	102	102
	102	(110)	108	104	100	100
4	120	(120)	118	122	120	118
	115	(120)	120	120	120	120
5	100	115	112	114	(110)	110
	104	(112)	110	106	108	106
			Control Subjects			
6	106	132	118	(112)	104	...
7	106	126	(102)	100	...	...
8	112	124	(118)	110	...	...
9	105	(110)	100	90	95	95
10	95	(105)	105	100	90	95
11	90	105	(100)	102	98	95
12	108	126	124	(118)	118	114
13	105	125	120	(115)	108	102
14	104	122	(112)	108	108	108
15	120	134	132	(122)	122	120

work,[13] whereas the earliest symptom of most varieties of cardiac dysfunction is respiratory difficulty rather than fatigue of the voluntary muscles.

13. Lewis, T.: Diseases of the Heart, New York, The Macmillan Company, 1934.

Our study of exercise tolerance in anemic children confirms these general impressions. It has already been indicated that figures obtained during the tests, especially those related to blood pressures, show so much variation as to make interpretation difficult. Similar fluctuations during and after the third minute following exercise were seen among the normal control subjects as well, and it is clear that the exercise tolerance test has its limitations when employed in the examination of children. However, the results are sufficiently clear to enable us to reach certain broad conclusions. There is a distinct contrast between the responses of the patient with acute and of those with chronic anemia. The former child showed an impairment of tolerance which

TABLE 5.—*Effect of Treatment on Vital Capacity*

Case No.	Height, Cm.	Before Treatment		After Treatment	
		Vital Capacity, Cc.	Vital Capacity/ Height	Vital Capacity, Cc.	Vital Capacity/ Height
		Anemic Subjects			
1	114.0	900	7.90	900	7.90
2	118.5	650	5.49	900	7.59
3	106.7	700	6.56	820	7.68
4	86.0	500	5.81	600	6.98
5	114.3	820	7.18	820	7.18
		Control Subjects			
6	133.4	1,600	12.00		
7	124.5	1,450	11.64		
8	143.0	2,100	14.68		
9	133.5	1,820	13.62		
10	138.4	1,700	12.28		
11	115.0	1,100	9.57		
12	119.3	1,750	14.66		
13	113.0	800	7.08		
14	121.9	1,100	9.03		
15	114.0	1,200	10.52		

was much greater than that of the latter patients. Such a difference in behavior might be expected, since those with chronic anemia had a long time in which to adapt themselves to the deficiencies of their blood supplies, while such a compensatory period was lacking for the child in whom the onset of anemia was acute. On the other hand, the relatively normal results of exercise tolerance tests of the children with chronic anemia were astonishing in view of their obvious signs of cardiac damage, for the hearts of all of these children were enlarged, in 2 cases enormously (cases 2 and 3); all had murmurs, and all had rapid rates, in 2 cases with gallop rhythm (cases 2 and 3). In case 2 the patient was admitted to the hospital with frank cardiac failure, as shown by markedly increased venous pressure, an enlarged, tender liver and edema of the ankles. The exercise tolerance test in this case was not performed until all evidence of failure had disappeared, after a period of rest in bed.

Since according to the exercise tolerance test the capacity of the patients with chronic anemia was little diminished, it is apparent that the usual criteria of change in pulse rate, blood pressure and respiratory rate cannot be used for measuring either the severity of the cardiac lesion resulting from anemia or the effect of transfusion on the heart.

The vital capacity in anemia is said to be normal or only slightly reduced.[12b] All of our patients, however, had vital capacities which were considerably smaller than either those of our control subjects or those of normal subjects reported on in the literature.[14] The capacities of our patients usually increased after treatment, an especially marked increase occurring in the case of the child admitted with congestive heart failure (case 2). These measurements of vital capacity are not altogether satisfactory, for there is undoubtedly a knack of using the spirometer to the fullest advantage, and it is almost impossible to judge at what point the child acquires this facility. For this reason we do not feel justified in using a test in which there is such a strong subjective factor as a basis for our assessment of cardiac damage.

CONCLUSIONS

With acute anemia the tolerance of the child for exercise is decreased, whereas with chronic anemia adaptation to the low hemoglobin concentration may be so complete that practically no impairment of exercise tolerance results.

Neither the exercise tolerance test nor measurements of vital capacity are sufficiently accurate or reliable to serve as a measure of the degree of cardiac damage resulting from anemia or to gage the ability of the heart to recover from such damage through appropriate treatment.

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14. Edwards, D. J., and Wilson, M. G.: An Analysis of Some of the Factors of Variability in the Vital Capacity Measurements of Children, Arch. Int. Med. **30**:638 (Nov.) 1922.

BASAL METABOLIC RATE IN CHILDREN WITH ABNORMAL BODILY DIMENSIONS

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For the last twenty-five years the basal metabolic rate of the normal child has been elaborately studied in numerous laboratories and clinics. Though the results of the various workers still show considerable divergence, the differences have markedly diminished in the investigations of recent years. Thus the results of Lewis, Kinsman and Iliff [1] show a striking correspondence with those of Bierring [2] and with mine. For an exhaustive review of the literature on the basal metabolic rate of the normal child, the reader is referred to the recent work of Lewis and his collaborators.[1]

The question of how to interpret the basal metabolic rates of children with abnormal bodily dimensions has not yet been satisfactorily answered. Among these children one must consider those with too large or too small a weight for their height and well proportioned children who are much too tall or too short for their age. One must exclude children whose abnormal measurements can be definitely ascribed to a clinically familiar disturbance of internal secretion, such as too small or too fat children with hypothyroidism.

The way in which the basal metabolic rate is to be interpreted for children with abnormal dimensions is intimately related to the question of whether and to what extent an excess of fatty tissue affects the basal metabolism and, further, to the question of whether age plays a part in determining the metabolic rate. The heat produced by the resting organism is almost exclusively manufactured by the so-called active protoplasm, i. e., by the muscles, the internal organs and the glands. Bones, tendons, body fluids and fatty tissue can be considered inactive. So it is clear that for a child with an excess of fatty tissue the rate cannot be calculated in the usual way, in accordance with the body weight. Nor is one justified in applying in this case a calculation

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1. Lewis, R. C.; Kinsman, G. M., and Iliff, A.: The Basal Metabolism of Normal Boys and Girls from Two to Twelve Years Old Inclusive, Am. J. Dis. Child. **53**:348 (Jan.) 1937.

2. Bierring, E.: The Standard Metabolism of Boys (Seven to Eighteen Years Inclusive), Copenhagen, Levin & Munksgaard, 1931.

according to the body surface, as Rubner's assumption of a close relation between heat production and body surface has been proved untenable (Wetzel [3]).

The solution of this problem is the more urgent because the disorders in which a knowledge of the basal metabolic rate is most important for diagnosis as well as for treatment are those connected with disturbance of internal secretion, in which the normal bodily proportions are often disarranged. Thus one is confronted with an equation which has two unknowns: first, the interpretation of the basal metabolic rate of an abnormally fat child; second, the extent to which the adiposity in this case must be ascribed to an endocrine disorder.

About ten years ago I began to estimate the basal metabolic rates of children of ages ranging from about 2 to 13 years in order to establish a standard curve for normal children. Since that time I have had repeated opportunities to examine also children with abnormal dimensions. With the aid of these measurements it has been possible to outline a provisional scheme for the interpretation of the basal metabolic rate for children of the latter type.

REVIEW OF THE LITERATURE

The interpretation of data from the literature for comparison with my results is difficult for two reasons: 1. Some of the papers on this subject give insufficient data and do not give the necessary information on the method of computing the basal metabolic rate. 2. A strict distinction has not always been made between undernourishment and thinness and between overnourishment and obesity. Such a distinction, however, is necessary, as my subject concerns children who remain too thin or too fat in spite of a normal diet and are therefore constitutionally abnormal. In undernourishment and overnourishment other factors are involved, as it is possible to influence the level of the basal metabolism by nutritional variations. Anderson and Lusk [4] in experiments on dogs found a persistently lowered basal metabolic rate after a period of fasting. Helmreich [5] stated the belief that the basal metabolic rate depends on the previous intake of food. Odin and Werdinius [6] found a decrease in the basal metabolic rate in a population whose diet consisted of milk, flour, potatoes and butter. The cause of this was

3. Wetzel, N. C.: On the Motion of Growth, J. Pediat. **3**:252, 1933.

4. Anderson, R. J., and Lusk, G.: Animal Calorimetry, J. Biol. Chem. **32**:421, 1917.

5. Helmreich, E.: Der "Grundumsatz" eine relative Grösse, Biochem. Ztschr. **146**:153, 1924.

6. Odin, M., and Werdinius, E.: Level of Basal Metabolism as Related to the Composition of the Diet, Acta med. Scandinav. **81**:249, 1934.

in all probability a comparatively low caloric content of the diet as well as nitrogen deficiency. In the investigations of Johnston and Maroney [7] a definite lowering of the metabolic rate was constantly evident with submaintenance diets. While with increased intake the basal heat production could in most subjects be brought from subnormal to normal levels, only slight increases beyond normal were evident. Added protein produced marked increases in rate.

The basal metabolism of obese children was observed by various workers, among them Langmead and Calvert,[8] who made a study of 8 boys and 4 girls in 1924, and by Topper and Mulier,[9] who investigated 78 subjects in 1929. In addition, Talbot and his associates [10] studied 35 new cases in 1937; the children were between 20 and 33 per cent overweight. Moreover, Talbot compared measurements for a group of 12 extremely obese children (from 33 to 80 per cent overweight for their height) with the normal standards. There was little change in the average figures when calories were referred to weight, but there was an increasing difference with increasing obesity when calories were referred to height. The weight standard seemed to give a more accurate picture than the height standard. In one paper Talbot [11] expressed the opinion that unless weight is approximately average for height and sex, metabolic data cannot be compared with any standard in which the total heat production is divided by the weight. This author stated that in actual practice it is more satisfactory to compare the data obtained from fat or thin children with both weight and height tables and to estimate the significance of the figures from the discrepancy between the two standards. Morgan and Hatfield [12] studied 5 children who were overweight for their height and age. Three showed an abnormally low metabolic rate and 2 had a normal rate, compared with the weight and surface standards proposed by Benedict and Talbot.

7. Johnston, J. A., and Maroney, J. W.: Basal Metabolism in the Period of Growth with Relation to the Previous Diet, Am. J. Dis. Child. **50**:1336 (Nov.) 1935.

8. Langmead, F. S., and Calvert, E. G. B.: Obesity in Children, Lancet **2**: 1111, 1924.

9. Topper, A., and Mulier, H.: Basal Metabolism of Children of Abnormal Body Weight: Basal Metabolism of Overweight Children, J. A. M. A. **92**:1903 (June 8) 1929.

10. Talbot, F. B.; Wilson, E. B., and Worcester, J.: Physiologic Background and Application of Standards, Am. J. Dis. Child. **53**:273 (Jan.) 1937.

11. Talbot, F. B.: Interpretation of the Basal Metabolism of Children, J. Pediat. **3**:246, 1933.

12. Morgan, A. F., and Hatfield, G. D.: The Basal Metabolism and the Specific Dynamic Action of Foods in Children in Various Conditions of Nutrition, Am. J. Dis. Child. **32**:516 (Oct.) 1926.

Lax and Petenyi [13] determined the basal metabolic rates of 14 adipose children with Krogh's gas apparatus. The results showed that the basal metabolic rates of obese children of adolescent age are decreased. As I could not get the original paper, I cannot say with what standards the results were compared. From the result of basal metabolic tests made on 70 overweight children Topper and Mulier [9] concluded that the majority of overweight but otherwise normal children have normal basal metabolic rates, with a tendency toward high normal rates.

The basal metabolism in underweight children was studied by Blunt, Nelson and Oleson,[14] among others. They reported on a series of 28 children, for whom they found high total metabolic rates, as calculated on the basis of the Benedict-Talbot weight standards. Wang, Kern, Frank and Hays [15] studied 14 boys and 18 girls. They found that underweight children adhere to the figures for age and height more closely than normal children. According to weight, the basal metabolic rates of underweight children were increased above normal but showed no relation to the degree of underweight. Topper and Mulier [16] studied 70 underweight children. As in their study of overweight children, they used as prediction standards only those which are based on a linear formula. The majority of the underweight children had normal basal metabolic rates, with a decided tendency toward low normal rates. In children becoming increasingly underweight, there was greater lowering of the basal metabolic rates. When they were more than 25 per cent underweight, the basal metabolic rates fell below the lowest normal limit, — 10. According to Talbot, slightly underweight children tend to have normal or rather high metabolic rates for their weight and rates lower than normal for their height. Two of the 4 underweight girls tested by Morgan and Hatfield showed nearly normal rates by all standards. The other 2 had high rates.

Up to the present, tall and short children of average weight for their height have not been studied extensively. According to Talbot, measurements obtained from these children are comparable with standards of calories per square meter, calories per kilogram and total

13. Lax, H., and Petenyi, G.: Basal Metabolism in Adipose Children at the Age of Puberty, Orvosi hetil. **71**:228, 1927; abstracted, Am. J. Dis. Child. **33**:986 (June) 1927.

14. Blunt, K.; Nelson, A., and Oleson, H. C.: The Basal Metabolism of Underweight Children, J. Biol. Chem. **49**:247, 1921.

15. Wang, C. C.; Kern, R.; Frank, M., and Hays, B.: Metabolism of Undernourished Children, Am. J. Dis. Child. **32**:350 (Sept.) 1926.

16. Topper, A., and Mulier, H.: Basal Metabolism in Children of Abnormal Body Weight: In Underweight Children, Am. J. Dis. Child. **38**:299 (Aug.) 1929.

calories for height and weight. Rosenblüth [17] found the metabolic rates of dwarfs only apparently increased. If the expected weight was referred not to the actual rate but to that corresponding to the age, the difference was smaller. In 2 chondrodystrophic dwarfs, normal basal metabolic rates were found to correspond to the expected weights. Topper [18] recorded studies on the basal metabolism of 20 children who were greatly retarded in growth but normal in all other respects. The figures obtained did not agree with any of the usual standards except that of the total calories referred to age. It was suggested by Topper that although normally this standard is not the best, the reason that underdeveloped children conform to it is as follows: While their physical proportions have remained underdeveloped, the growth of the inner organs and therefore the actual cellular activity of the body have proceeded normally, agreeing with their age. There is no reason at all to accept this hypothesis as true. On the contrary, at autopsy one gets an impression that in case of retarded growth the internal organs partake in this retardation. Moreover, it cannot be true, simply for the reason that the muscular mass, at least, must remain less in accordance with the retarded general growth.

PROCEDURE

Apparatus.—I made my estimations with the apparatus of J. G. Dusser de Barenne and G. C. E. Burger. This has been described in detail.[19] It is an apparatus by which only the gas exchange by the lungs is measured, both oxygen and carbon dioxide being determined, and in which analysis of the gas is not required.

A brief exposition of the principles of this construction will suffice. In figure 1, two Krogh recorders of breathing volume are represented by *1* and *2*. This type of recorder or spirometer consists of a rectangular double-walled box, the space between its walls being filled with water. In the water between the walls a roof-shaped cover is kept floating; this is fastened in such a way that it rotates on an axis formed by one of the short upper edges of the spirometer box. The cover is counterbalanced by a weight. When the lower edges of the cover are immersed, the space within the spirometer is shut off and rendered air tight. By two tubes (*c* and *d*) spirometer *1* is connected with the outer world. Spirometer *2* is constructed similarly to *1*, but on its floor is adjusted a wire netting covered with a thin layer of soda lime. Moreover, to this tank a side tube with a tap is adjusted for the supply of oxygen. *M* represents a mouth piece mounted on a T-shaped metal tube, both ends of which are encased in a glass bell containing

17. Rosenblüth, A.: Basal Metabolism in Children and Adolescents During Disease, Ztschr. f. Kinderh. **49**:118, 1930.

18. Topper, A.: Standards of Basal Metabolism for Children of Retarded Growth, Am. J. Dis. Child. **45**:1203 (June) 1933.

19. Abderhalden, E.: Handbuch der biologischen Arbeitsmethoden, Berlin, Urban & Schwarzenberg, 1927, vol. 10, pt. 4, pp. 937-984.

the valves for inspiration and expiration, respectively. *A* represents a Tissot spirometer. This consists of a bell suspended in water and accurately outbalanced, so that if one breathes into the spirometer the bell rises. The whole again is enclosed in an air-tight tank, which is connected with recorder *1* (fig. 2). On the covers of both Krogh spirometers are mounted writing levers (*S1* and *S2*), which register the movements of the covers on a kymograph (*k*). The various parts of the apparatus are further connected by rubber tubes, and the direction of the flow of air can be changed at will by three way cocks. Moreover, between

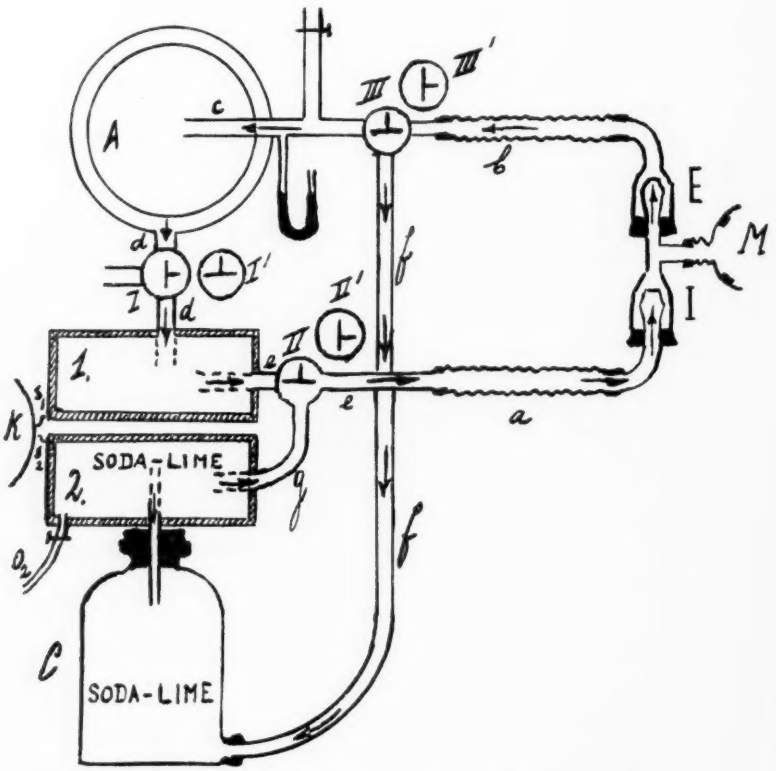

Fig. 1.—Diagram of the apparatus of Dusser de Barenne and Burger.

spirometer *2* and the expiration valve is interposed a Mariotte flask (*C*) which is almost completely filled with soda lime.

The measuring proceeds as follows: The subject takes the mouth piece, *M*, in his mouth; the cavity of the mouth is thus brought into air-tight connection with the apparatus. A nose clamp provides for air-tight obturation of the nose (fig. 3). At the beginning of the procedure the three way cocks are put in positions *II* and *III* (fig. 1). By the inspiration valve, *I*, the subject breathes air from spirometer *1* by way of tube *a*, tube *e* and cock *II*, the connection with spirometer *2* being shut off. The expired air goes to spirometer *A* by expiration valve *E*, tube *b*,

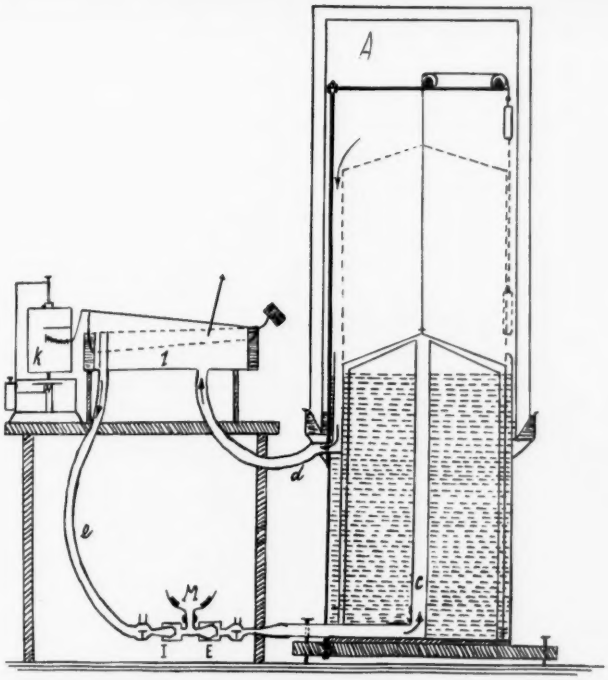

Fig. 2.—Diagram of the portion of the apparatus of Dusser de Barenne and Burger by which carbon dioxide is estimated.

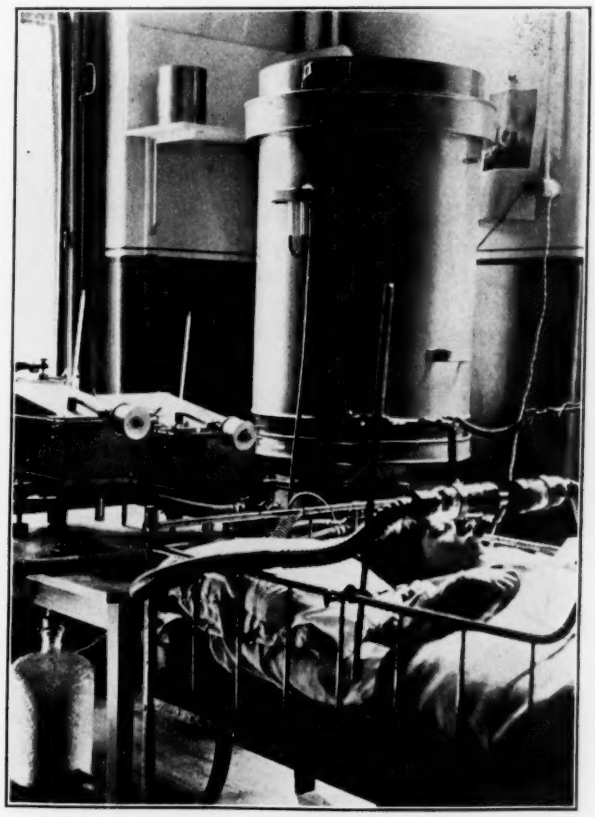

Fig. 3.—The apparatus of Dusser de Barenne and Burger in use.

cock *III* and tube *c*. The bell of *A* is raised, and a volume of air equal to that breathed into the bell is reconducted to spirometer *1* by tube *d* and cock *I*. In this way the writing lever *S1* produces an up and down curve on the kymograph, which I shall call the carbon dioxide curve (fig. 4 *B;* to be discussed later).

When after some time the cocks are returned from positions *II* and *III* to *II'* and *III'*, the large spirometer, *A*, and recorder *1* (the Krogh carbon dioxide spirometer) are put out of circulation, so that the subject breathes out of recorder *2* (the Krogh oxygen spirometer), which has been filled with oxygen. The inspiratory air is led from Krogh spirometer *2*, tube *g*, three way cock *II'*, tube *e* and rubber tubing *a* by inspiration valve *I* to the subject's mouth. The expiratory air proceeds by expiration valve *E*, tube *b*, cock *III'*, tube *f* and bottle *C* (where all the carbon dioxide is captured by soda lime) back to spirometer *2*, in which possible remnants of carbon dioxide are fixed by a layer of soda lime at the bottom.

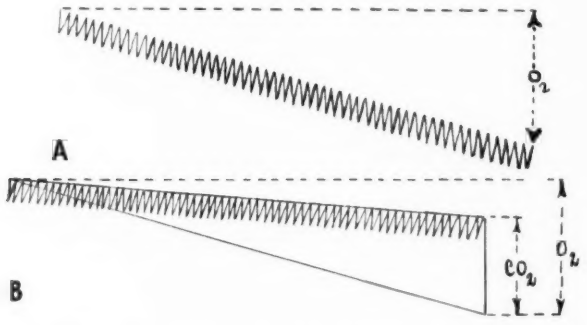

Fig. 4.—*A*, the oxygen curve. *B*, the carbon dioxide curve compared with the oxygen curve.

The quantity of the oxygen intake and of the carbon dioxide output are now calculated. Figure 4 *A* represents an oxygen curve, recorded by the process of rebreathing into Krogh spirometer *2*. The fall in the level of the curve indicates the amount of oxygen absorbed by the subject during the time of examination, the carbon dioxide substituted for the oxygen by the body being excluded from the spirometer by the action of the soda lime. The recorder of the breathing volume has previously been standardized as to the amount of oxygen represented by a given fall of the curve. For a usable curve it is necessary that the subject breathe quietly and regularly, so that the tops of the curve all lie on a straight line. If the curve is irregular, an estimation of the oxygen intake is impossible and the experiment is a failure.

The amount of the carbon dioxide output is found by subtracting the decline of the carbon dioxide curve from that of the oxygen curve. This can be explained as follows: If the subject did not produce any carbon dioxide at all, the carbon dioxide curve would show the same decline as the oxygen curve. Because of the carbon dioxide actually produced, the fall of the carbon dioxide curve becomes less steep than that of the oxygen curve; this difference in decline indicates the amount of carbon dioxide produced during the experiment (fig. 4 *B*).

From the results of both curves one can calculate the respiratory quotient, and knowing this one can determine the caloric output with the help of the table of Zuntz and Geppert, which gives the caloric equivalent for 1 liter of oxygen for every respiratory quotient between 0.7 and 1.

Technic.—In order to obtain standard curves, 120 boys and 123 girls were examined, all of them between the ages of 1 and 16 years. I could work only with children staying in the hospital, among whom were selected those who had regained perfect health. The estimation was carried out during the last days of their stay. Only those children were examined whose basal metabolism supposedly was not influenced by the preceding illness or convalescence.

In this respect the present study differed from the work of others, who have carefully selected normal children for their estimations. I do not think this difference to be a disadvantage in establishing standard curves, for my aim was not primarily to collect strictly physiologic data but to draw up curves that can be used in clinical examination. In clinical practice a physician wants to know the basal metabolism of children as they actually are: there is no possibility of a previous selection of subjects.

The children had preliminary training on the day before the test. On the morning of the test they were left fasting, were not washed or otherwise interfered with and remained quietly in bed till they were carried to the examination room. Here they were also left quietly in bed for twenty to thirty minutes before the experiment was begun. For some time I have omitted the training on the previous day with older children and have used the time of quiet waiting in the examination room before the experiment for this training, which saves time and does not impair the results. For each child estimations were made on at least two days; the number of estimations for each child was at least four. For the great majority of children several more examinations were made, generally six to ten, sometimes more. Most of the children were examined on three or four days. If no difficulties were met with, for each child six carbon dioxide curves of four minutes each were made in a day, and between them four oxygen curves of three minutes each.

In this way I succeeded in examining the children under actually basal conditions. For some of the children the examination failed, but their number was relatively small. In Talbot's opinion it is not possible to determine the metabolic rate of children less than 7 years old under actual basal conditions with types of apparatus requiring a mouth piece and a nose clip. This was not found to be true. I even succeeded in examining children weighing only 7 to 9 Kg. Extremely young children, after some resistance, resigned themselves to the procedure; most of them eventually fell asleep. This enabled me to study the basal metabolism of young children during sleep.[20] As the rate decreases during sleep, I have not utilized the figures thus obtained in drawing up the standard curves.

RESULTS

In tables 1 and 2 are represented the results of estimations of the basal metabolic rates for 120 normal boys and 123 normal girls. In figure 5 they are plotted in curves according to the body weight. Orig-

20. de Bruin, M.: Respiration and Basal Metabolism in Childhood During Sleep, Acta pædiat. **18**:279, 1936.

inally I made curves of the basal metabolic rates as judged by body surface, length and weight and also as calculated per kilogram of body weight and per square meter of body surface. These curves are not

TABLE 1.—*Basal Metabolic Rates of Normal Boys*

Age		Height,	Weight,	Basal Metabolic Rate, Calories per	Age		Height,	Weight,	Basal Metabolic Rate, Calories per
Yr.	Mo.	Cm.	Kg.	24 Hours	Yr.	Mo.	Cm.	Kg.	24 Hours
1	2½	74.0	8.50	614	7	10	121.5	19.55	883
1	3	76.0	9.60	669	7	11	120.0	22.30	1,004
1	3½	76.0	9.60	720	8	..	119.0	21.15	960
1	4	68.0	6.30	554	8	..	141.5	31.80	1,256
1	5	72.0	9.40	679	8	2	124.0	23.85	972
1	5½	74.0	7.85	589	8	2½	125.5	27.90	1,175
1	5½	81.0	10.50	605	8	3	112.0	22.10	1,055
1	6	79.0	11.00	695	8	3	128.5	24.60	1,133
1	7	83.0	10.40	796	8	3	120.0	21.10	1,032
1	7½	79.0	9.60	535	8	7	130.0	28.40	1,094
1	9	77.0	8.90	657	8	8	128.0	26.10	1,263
1	9	83.0	9.70	566	8	9	133.0	25.60	1,054
1	11	82.0	11.50	648	8	9	133.0	24.60	1,067
1	11½	71.0	7.20	574	8	9	124.5	24.40	1,175
2	1	83.5	12.45	597	8	10½	129.0	26.00	1,133
2	2	73.0	7.50	565	9	1	129.0	26.20	1,038
2	3½	80.5	10.70	719	9	1	98.5	14.70	803
2	4	82.0	10.90	668	9	2½	132.0	26.40	1,109
2	5	90.5	12.60	872	9	7½	124.5	26.20	1,142
2	5	100.0	15.20	747	9	9	127.0	24.90	1,049
2	10	89.0	13.50	842	10	..	130.0	29.80	1,190
2	11	87.0	13.20	848	10	1	136.0	28.40	1,140
3	½	90.0	12.15	729	10	2	132.5	30.15	1,173
3	2	91.0	13.70	838	10	3	140.5	30.00	1,190
3	2	92.0	14.50	845	10	4½	143.5	32.30	1,351
3	2½	94.0	15.65	750	10	6½	144.5	30.20	1,152
3	3½	94.0	14.90	884	10	7	144.0	34.80	1,281
3	3½	99.0	13.15	783	10	8	135.0	34.30	1,305
3	3½	87.0	12.10	737	10	8½	138.5	36.70	1,388
3	6	95.0	13.60	940	11	..	141.5	28.35	1,168
3	6½	92.0	12.80	756	11	1	140.0	37.90	1,118
3	7	91.0	12.80	747	11	1½	141.5	37.70	1,333
3	7½	98.5	16.30	854	11	2	138.0	34.80	1,199
3	8	96.0	14.10	780	11	3½	152.0	42.50	1,428
3	10½	81.0	11.90	820	11	4	137.0	31.30	1,360
4	3	103.0	19.25	863	11	4	158.0	37.50	1,377
4	4	87.0	11.50	731	11	6	130.0	30.00	1,163
4	4½	95.5	14.50	860	11	6	151.0	35.80	1,331
4	6	109.0	17.35	849	11	6½	145.5	32.90	1,050
Under 5	..	101.0	16.50	881	11	7	142.0	37.50	1,403
5	..	107.0	18.05	946	11	7	142.5	32.30	1,316
5	1½	105.0	16.60	822	11	8½	147.5	35.70	1,174
5	2	99.0	16.10	836	11	9	151.0	38.00	1,314
5	5	109.0	17.50	905	12	..	150.0	40.40	1,419
5	7½	113.0	22.15	980	12	1	151.0	40.60	1,333
5	8	110.0	18.80	969	12	1	141.0	32.60	1,232
5	10	126.5	28.30	1,074	12	3	151.0	51.40	1,357
5	10½	111.0	19.70	861	12	4	151.5	34.90	1,252
6	5	108.0	18.15	930	12	7	136.0	30.80	1,143
6	5½	99.0	19.15	895	12	7	148.0	31.50	1,116
6	5½	123.0	19.60	1,049	12	7½	153.0	38.90	1,234
6	6	114.0	17.55	811	12	9½	153.0	38.55	1,437
6	8½	108.0	16.20	780	12	11	160.0	55.90	1,498
6	9	107.0	17.10	861	Over 13	..	141.0	31.50	1,348
6	9	110.0	16.85	915	13	1	145.0	35.60	1,264
7	..	115.0	21.30	1,011	13	8	151.5	40.50	1,433
7	1	125.0	22.60	1,042	13	10	147.5	34.60	1,311
7	4	111.5	17.10	962	14	..	158.0	42.45	1,260
7	7½	118.0	21.25	1,009	14	2	160.5	42.40	1,360
7	8	125.0	23.10	1,018	15	7	156.5	49.50	1,482

reproduced here because the calculation of the rate by body weight is the most rational and has proved to be the most reliable for children of normal size. Recently this problem has been extensively dealt with by Talbot, who arrived at the same conclusion.

1. *Abnormally Fat Children.*—It is not justifiable simply to discard the excess weight of the fat child and to calculate the basal metabolic rate according to the standard weight because the number of kilograms

TABLE 2.—*Basal Metabolic Rates of Normal Girls*

Age		Height,	Weight,	Basal Metabolic Rate, Calories per	Age		Height,	Weight,	Basal Metabolic Rate, Calories per
Yr.	Mo.	Cm.	Kg.	24 Hours	Yr.	Mo.	Cm.	Kg.	24 Hours
1	1	73.0	8.80	597	6	10	108.0	21.60	1,006
1	2	76.0	10.45	639	6	10½	104.0	14.50	747
1	2	79.0	10.35	540	6	11	85.0	12.00	603
1	2½	76.0	9.10	540	Under 7	..	112.0	18.90	956
1	5	72.5	7.70	618	7	4½	108.0	18.80	941
1	5½	73.5	7.80	584	7	5½	119.0	24.10	1,082
1	7	75.0	8.15	614	7	7	116.0	22.50	1,138
1	7½	81.5	9.70	643	7	8	114.0	17.95	858
1	7½	77.0	9.70	625	7	10	135.0	28.40	1,134
1	8	82.0	11.25	738	8	3	125.5	25.65	1,097
1	8½	82.0	11.20	604	8	3	127.0	23.25	954
1	9	79.5	9.30	681	8	5	121.0	24.90	1,150
1	10½	84.0	11.15	592	8	7	121.5	23.00	1,092
2	1	87.5	12.25	646	8	7	126.0	24.20	1,101
2	3½	80.5	11.15	591	8	7	133.0	34.10	1,102
2	4	84.0	11.00	641	8	11	137.0	29.80	1,212
2	5	85.0	11.40	687	Under 9	..	119.0	24.10	1,082
2	6	83.0	9.15	616	9	..	134.0	24.30	993
2	7½	74.0	10.15	746	9	2½	142.0	29.20	1,105
2	10	91.5	13.65	714	9	4	128.5	29.05	1,131
2	10	89.0	11.45	667	9	5	141.0	39.30	1,231
2	11	88.0	13.25	702	9	6	131.0	24.30	1,033
3	½	90.0	12.30	735	9	6	128.0	23.70	1,011
3	½	72.0	7.70	517	9	7	137.0	27.25	1,127
3	1	90.0	10.80	684	9	8	142.0	31.40	1,086
3	1	82.0	9.40	682	9	10	133.5	26.90	1,026
3	3	82.0	9.40	716	9	10	138.5	27.20	1,056
3	3	89.0	13.50	791	10	1	146.0	43.70	1,214
3	6½	99.0	15.40	809	10	2	141.5	38.30	1,242
3	9	104.0	15.60	756	10	3½	128.0	26.90	1,057
3	9	83.0	11.70	781	10	4	144.0	33.20	1,331
3	10	98.0	14.00	739	10	8	146.0	30.90	1,145
3	11	94.0	12.45	711	10	10½	142.5	29.60	1,109
3	11	94.5	13.25	676	10	11	144.0	29.40	1,081
4	2½	106.0	17.10	865	11	2	136.5	30.50	1,178
4	3	99.5	14.30	694	11	3	143.0	36.10	1,280
4	4½	105.0	17.10	904	11	5	134.5	30.40	1,084
4	6½	94.0	12.00	760	11	5	150.0	46.00	1,383
4	7½	95.5	13.90	774	11	7	147.5	39.10	1,328
4	8	97.5	14.50	815	11	7	140.0	36.20	1,142
4	11	111.0	19.60	849	11	8	143.0	39.20	1,326
5	3	111.5	23.60	958	11	8	149.0	39.30	1,349
5	3½	98.5	12.90	761	11	9	146.0	31.40	1,081
5	4½	106.0	16.40	934	11	10	137.0	29.70	1,131
5	5	101.0	15.70	801	11	11	132.0	28.30	1,181
5	6	106.0	17.65	904	11	11½	144.0	33.80	1,096
5	6	91.0	10.90	607	11	11½	154.0	39.60	1,343
5	8	95.0	12.25	697	Under 12	..	139.0	33.70	1,326
5	8	108.0	19.25	837	12	..	143.5	40.80	1,192
5	9	104.0	14.60	805	12	2	145.0	30.95	1,081
5	10	112.5	19.75	791	12	2½	140.0	28.10	995
Under 6	..	105.0	16.25	770	12	3	149.5	34.20	1,206
6	..	119.5	20.15	833	12	6	137.5	30.95	1,073
6	1	114.0	20.00	942	12	6	140.0	32.30	1,339
6	1½	95.5	14.50	785	13	..	152.0	36.90	1,405
6	2	104.0	15.65	770	13	10½	150.0	38.70	1,317
6	3	114.0	24.10	1,039	14	10½	158.5	53.20	1,306
6	9	126.0	21.80	979	15	2	145.0	42.60	1,366
6	9	121.0	27.75	1,044	15	8½	152.5	48.20	1,281
6	9	116.0	22.60	955	16	4½	160.0	52.10	1,514
6	10	116.0	20.60	1,041	16	9	157.5	47.00	1,262
					17	2½	156.0	55.40	1,448

thus subtracted should represent inactive tissue. In the first place, it is not known how far this inactivity goes, especially with extreme obesity. Moreover, it is probable that in the obese person the muscles eventually

tend to supernormal development, hypertrophy due to activity caused by the necessarily augmented use of energy during normal exercise. This must change the proportion between active protoplasm and inactive tissue.

One must look therefore for the criterion for judgment of the basal metabolism in obese children in a purely empiric way. It has been shown that the various workers mentioned in the review of the literature have obtained widely divergent results and that up to the present no

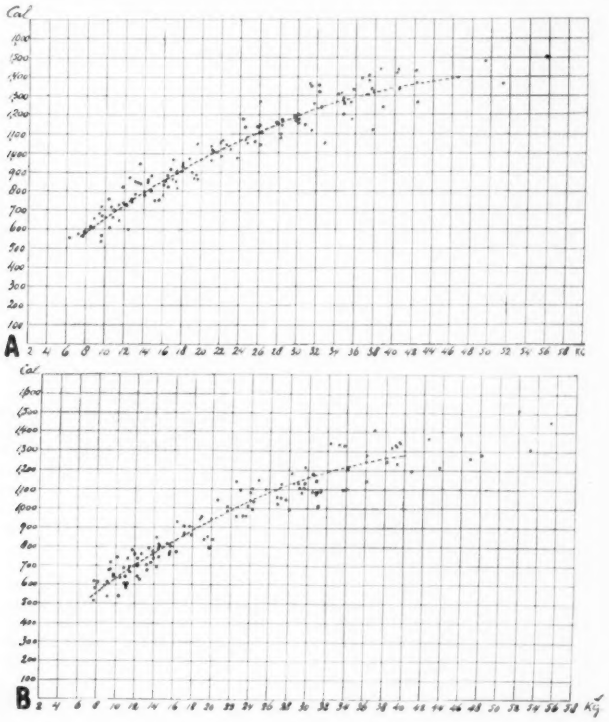

Fig. 5.—*A*, the basal metabolic rates of normal boys in calories per twenty-four hours referred to body weight. *B*, the basal metabolic rates of normal girls in calories per twenty-four hours referred to body weight.

agreement exists as to the problem of judging the basal metabolism in children of abnormal bodily proportions.

In my investigation I expressed the differences between the actual weight of fat or thin children and their standard weight according to their height in percentage of the standard weight. According to the amount of excess or shortage in height, three groups were distinguished: There were aberrations of 20 to 35 per cent, of 35 to 50 per cent and of over 50 per

TABLE 3.—*Basal Metabolic Rates of Fat Boys*

Age		Height,	Weight,	Standard Weight for Actual	Excess in Weight			Basal Metabolic Rate, Calories per
Yr.	Mo.	Cm.	Kg.	Height	Kg.	Percentage		24 Hours
9	4	131.0	33.70	28.2	5.50	20		1,270
11	5	150.0	47.20	39.0	8.20	21		1,383
5	8	110.0	24.30	19.7	4.60	23	○	1,107
11	7	143.5	45.10	34.5	10.60	31		1,406
Under 7	..	124.5	33.00	24.8	8.20	33		1,200
3	8	97.5	21.00	15.8	5.20	38		912
10	2½	141.0	47.00	33.3	13.50	41		1,333
6	8	120.5	33.15	23.3	9.85	42	△	1,107
9	6	132.0	41.50	28.5	12.90	45		1,185
8	7	132.0	42.30	28.5	13.80	48		1,223
8	..	129.0	41.40	27.3	14.10	52		1,210
6	5½	116.0	32.50	21.3	11.20	53	▲	1,093
5	5	105.0	28.10	18.0	10.10	56		1,020

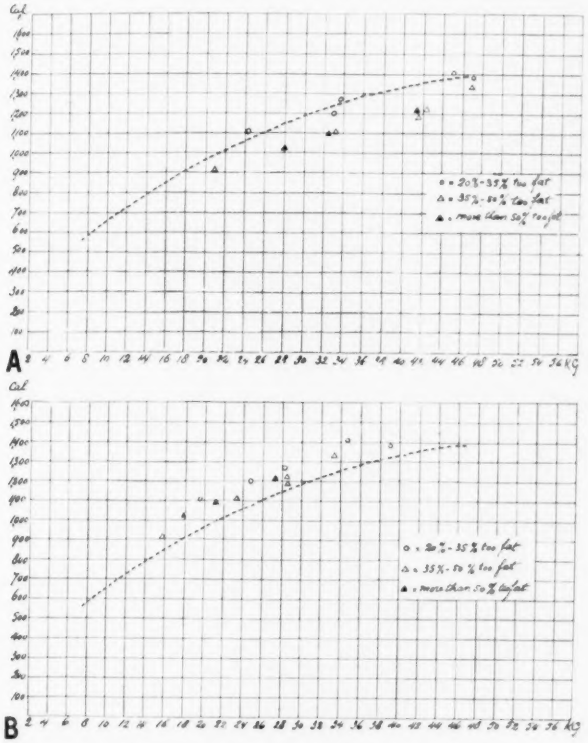

Fig. 6.—*A*, the basal metabolic rates of fat boys in calories per twenty-four hours referred to actual weight. *B*, the basal metabolic rates of fat boys in calories per twenty-four hours referred to standard weight according to actual height.

cent. In all, 13 obese boys were examined, 5 belonging to the first, 5 to the second and 3 to the third group. The results are given in table 3. In order to assess the influence of the inactive fat, I first put the figures calculated according to the actual weight against the standard curve (fig. 6 *A*). As could be expected, most of the points were far below the normal

curve. Only the results for boys belonging to the first group (excess of 20 to 35 per cent) fell within the normal range of variation. From this one may conclude that for boys no more than 35 per cent too fat the basal metabolic rate can be calculated in the ordinary way. This group therefore remains out of the scope of our subject.

TABLE 4.—*Basal Metabolic Rates of Fat Girls*

Age		Height, Cm.	Weight, Kg.	Standard Weight for Actual Height	Excess in Weight			Basal Metabolic Rate, Calories per 24 Hours
Yr.	Mo.				Kg.	Percentage		
5	2	109.0	23.10	19.3	3.80	20		900
5	2	116.5	27.85	21.8	5.85	23		962
13	½	149.0	48.40	39.4	9.00	23		1,398
9	½	141.0	41.60	33.5	8.10	24		1,207
11	9	140.5	41.50	33.3	8.20	25		1,211
8	2	135.0	38.30	30.2	8.10	27	○	1,148
10	5½	133.0	37.50	29.2	8.30	28		1,355
11	5½	140.0	42.70	33.2	9.50	29		1,487
11	8½	122.0	31.10	24.2	7.00	29		1,012
2	10	104.0	22.45	17.2	5.25	31		960
8	4	136.0	40.70	30.5	10.20	33		1,174
5	6	113.0	27.70	20.5	7.20	35		1,007
9	6	128.0	37.25	27.0	10.25	38		1,102
9	7½	140.0	45.70	33.2	12.50	38		1,298
12	5½	154.0	61.80	44.0	17.80	40		1,380
8	2½	125.0	35.30	25.3	10.00	40	△	965
13	..	156.0	65.30	46.0	19.30	42		1,490
9	3	127.0	37.50	26.3	11.00	42		930
10	4	136.0	44.30	30.5	13.80	45		1,107
7	11	129.5	39.90	27.5	12.40	45		1,258
8	6	128.0	40.85	27.2	13.65	50		1,077
Over 7	..	112.0	31.80	20.3	11.50	57	▲	870

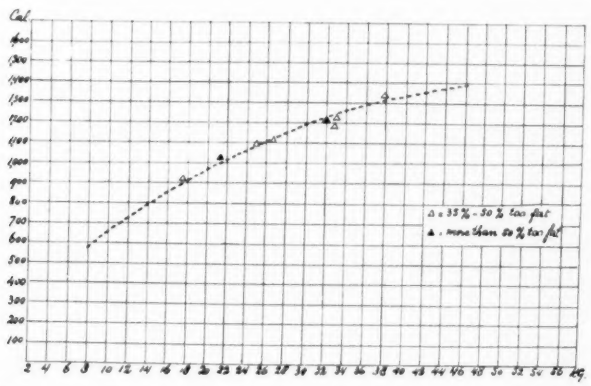

Fig. 7.—Basal metabolic rates of fat boys in calories per twenty-four hours referred to standard weight according to actual height increased by one third of the excess in weight.

Next, the results calculated after the standard weight according to actual height were plotted against the standard curve (fig. 6 *B*). All the points lay above the curve. By comparison of both graphs (fig. 6 *A, B*) it is seen that the basal metabolic rate can be calculated in such a way that all the points will fall within the normal range of variation; the basis

for such a curve is the standard weight increased by one third of the excess weight. Figure 7 shows this result; it does not show any material difference between the boys weighing 35 to 50 per cent and those weighing over 50 per cent too much. This might speak for the rationality of the method, though the number of observations is still too small for definite judgment.

The number of obese girls was 22, 11 belonging to the first, 9 to the second and 2 to the third group (over 50 per cent of excess). The results are given in table 4.

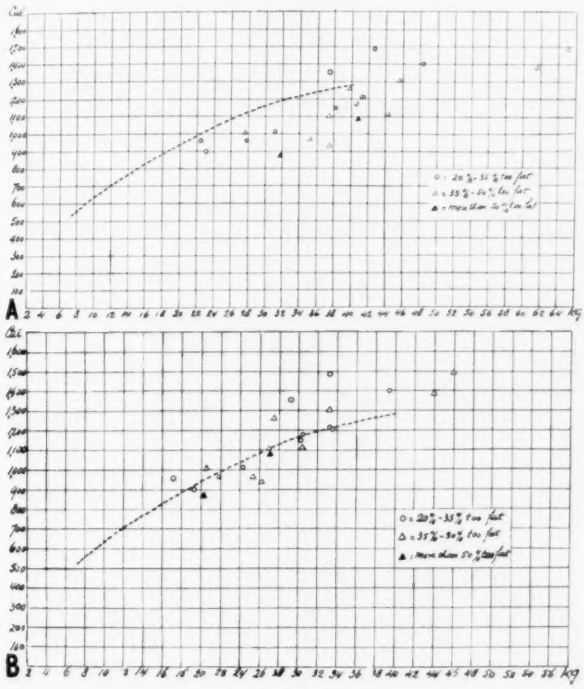

Fig. 8.—*A*, the basal metabolic rates of fat girls in calories per twenty-four hours referred to actual weight. *B*, the basal metabolic rates of fat girls in calories per twenty-four hours referred to standard weight according to actual height.

In many studies on basal metabolism it was found that the figures for girls showed a wider range of variation than those for boys. This further hampers one's attempts at clear judgment. The extent of the spreading of the values for girls was shown by Talbot [21] in 1936. On examining 70 normal girls he found for 5 per cent basal metabolic rates 15 to 20 per cent below normal and for 10 per cent rates 15 to 25 per cent above it.

21. Talbot, F. B.: Basal Metabolism of Girls, Am. J. Dis. Child. **52**:1 (July) 1936.

When the results calculated for obese girls according to their actual weight were plotted, the figures, like those for obese boys, were found to lie far below the standard curve. Only a few lay above it (fig. 8*A*). In contrast to the results for boys, even the figures for the first group (20 to 35 per cent overweight) lay for the most part below the curve. Subsequently I tried to find the right method of calculation by arranging the result in various ways, namely, according to the standard weight (fig. 8*B*), the standard weight increased by half of the excess weight and the standard weight increased by one third of the excess. After arranging the figures obtained by these various calculations in the form of frequency curves (as in measuring the erythrocyte size by the Price-Jones curve), I concluded that the calculation according to the standard weight increased by one third of the excess is the right method for girls (fig. 9) as well as for boys. The wide deviations shown by this diagram

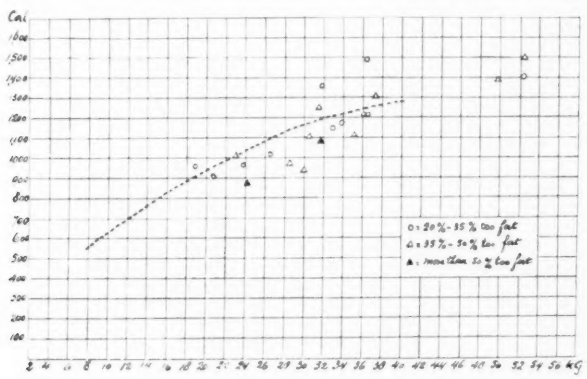

Fig. 9.—Basal metabolic rates of fat girls in calories per twenty-four hours referred to standard weight according to actual height increased by one third of the excess in weight.

may seem unsatisfactory at first sight, but they are of no greater order than those often found in similar studies on the basal metabolic rates of girls.

In contrast to the rates of boys of the corresponding group, the rates of girls 20 to 35 per cent overweight must also be calculated in this way. Perhaps this can be explained by the fact that a normally built girl has more subcutaneous fat than a boy of the same size, so that an excess of fat will sooner influence the basal metabolism.

2. *Abnormally Thin Children.*—The difference in weight between normal and thin children is mainly determined by the amount of fatty tissue. Therefore the basal metabolic rate of a thin child will probably have to be judged in quite another way than that of a fat child. It depends on the proportion between the amount of fatty tissue and that of other inactive tissues of the human body, such as tendons, bone and

body fluids. If the amount of fat is normally relatively small, it is not impossible that for a thin person the basal metabolic rate can simply be calculated by the actual weight. In this case one disregards the possibility that for a thin but otherwise normal person the standard for the basal metabolic rate should be established on another level.

I examined 6 thin boys who were otherwise healthy and were not undernourished. They weighed 20 to 35 per cent less than normal. The results are given in table 5. According to the standard weights, the basal metabolic rates of all lay below the standard curve (fig. 10 *A*);

TABLE 5.—*Basal Metabolic Rate of Thin Boys*

Age		Height, Cm.	Weight, Kg.	Standard Weight for Actual Height	Shortage in Weight		Basal Metabolic Rate, Calories per 24 Hours
Yr.	Mo.				Kg.	Percentage	
9	8	144.0	28.30	35.2	6.90	20	1,007
Under 10	..	149.0	30.50	38.5	8.00	21	1,217
14	6	163.0	41.40	52.2	10.80	21	1,320
2	..	93.0	11.30	14.5	3.20	22	738
4	9	98.5	12.70	16.4	3.70	23	791
15	2	166.5	42.65	55.9	13.25	34	1,521

TABLE 6.—*Basal Metabolic Rate of Thin Girls*

Age		Height, Cm.	Weight, Kg.	Standard Weight for Actual Height	Shortage in Weight		Basal Metabolic Rate, Calories per 24 Hours
Yr.	Mo.				Kg.	Percentage	
13	5	163.0	42.20	52.7	10.50	20	1,208
4	8½	100.0	12.95	16.2	3.35	21	656
6	½	105.0	13.55	17.4	4.00	22	812
6	3	93.0	10.90	14.0	3.10	22	641
14	9	151.5	32.40	41.7	9.30	22	1,243
5	10	95.0	11.30	14.7	3.40	23	659
9	1	130.0	20.85	27.6	6.75	24	777
10	9	146.0	27.95	37.3	9.35	25	985
Under 7	..	94.0	10.60	14.3	3.70	26	646
8	..	96.5	11.30	15.2	3.90	26	631

according to the actual weights, the rates of all lay within the normal range (fig. 10 *B*). Although this small number of cases does not permit a precise conclusion, it will be presently shown that for 10 thin girls the same result was reached. So one may assume that for a thin boy the basal metabolic rate can be calculated in the usual way, by the actual weight, as was to be expected.

Ten thin girls were examined; they were 20 to 35 per cent underweight. The results are found in table 6. For this group likewise calculations based on the standard weights would make all values fall far below the standard curve (fig. 11 *A*). A calculation based on the actual weights is given in fig. 11 *B*. For 8 of the 10 subjects the figures are certainly within the normal range; for the other 2 the figures reached

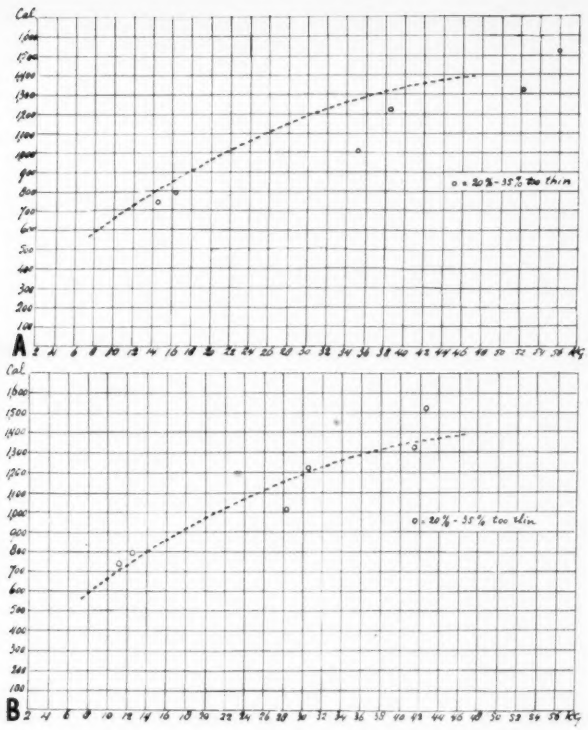

Fig. 10.—*A*, the basal metabolic rates of thin boys in calories per twenty-four hours referred to standard weight according to actual height. *B*, the basal metabolic rates of thin boys in calories per twenty-four hours referred to actual weight.

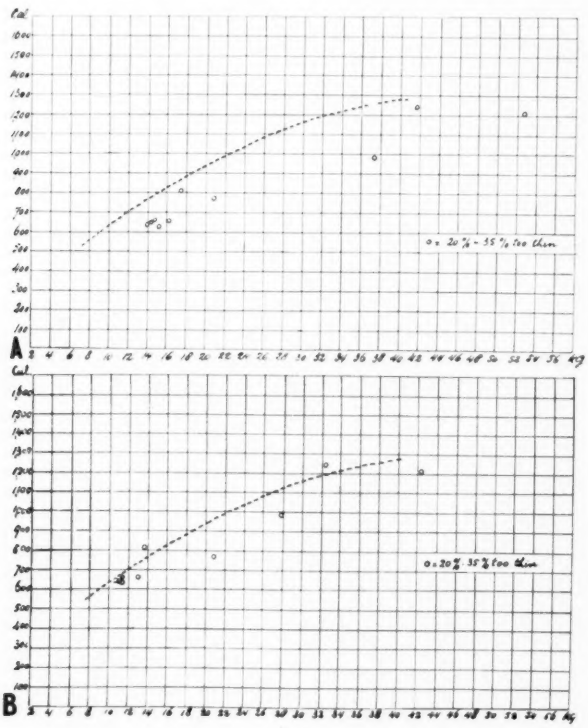

Fig. 11.—*A*, the basal metabolic rates of thin girls in calories per twenty-four hours referred to standard weight according to actual height. *B*, the basal metabolic rates of thin girls in calories per twenty-four hours referred to actual weight.

the lower limit. Future work will decide whether a small correction will still be necessary for thin children. Such a correction would agree with the opinion of those workers who think that the basal metabolic rates of thin persons lie on a lower level. Provisionally, I should calculate the rates simply by the actual weight.

3. *Well Proportioned Children of Abnormal Height.*—Calculating the basal metabolic rates for these children depends only on the problem

TABLE 7.—*Basal Metabolic Rates of Tall Boys*

Age		Height,	Weight,	Standard Height	Excess in Height			Basal Metabolic Rate, Calories per 24 Hours
Yr.	Mo.	Cm.	Kg.	for Age	Cm.	Percentage		
3	3½	99.0	13.15	93.0	6.0	7		783
11	8½	147.5	35.70	138.0	9.5	7		1,174
6	5½	123.0	19.60	114.0	9.0	8	○	1,049
10	4½	143.5	32.30	133.0	10.5	8		1,351
10	7	144.0	34.80	134.0	10.0	8		1,281
11	9	151.0	38.00	139.0	12.0	9		1,314
11	3½	152.0	42.40	136.0	16.0	12		1,428
2	5	100.0	15.20	87.0	13.0	15	△	747
5	10	126.5	28.30	109.0	17.5	16		1,074
8	..	141.5	31.80	122.5	19.0	16		1,255

TABLE 8.—*Basal Metabolic Rates of Short Boys*

Age		Height,	Weight,	Standard Height	Shortage in Height			Basal Metabolic Rate, Calories per 24 Hours
Yr.	Mo.	Cm.	Kg.	for Age	Cm.	Percentage		
1	2½	74.0	8.50	79.0	5.0	6		614
2	3½	80.5	10.70	86.0	5.5	6		719
1	9	77.0	8.90	83.0	6.0	7	○	657
3	3½	87.0	12.00	93.0	6.0	7		737
12	7	136.0	30.80	146.0	10.0	7		1,143
1	5½	74.0	7.85	81.0	7.0	9		589
1	5	72.0	9.40	81.0	9.0	11		679
4	4	87.0	11.50	99.0	12.0	12		731
6	5½	99.0	19.10	114.0	15.0	13		895
2	2	72.5	7.50	84.5	12.0	14	△	565
1	4	68.0	6.30	80.0	12.0	15		554
1	11½	71.0	7.20	84.0	13.0	16		574
3	10½	81.0	11.90	97.0	16.0	17		820
9	1	98.5	14.70	126.0	27.5	22	▲	803

of whether age as such influences the rates. If it does not, the rates can be judged simply by the body weights, in the usual way. Talbot thinks that this method of calculation is justified. As I am of the same opinion, I have estimated the rates of well proportioned but too tall or too short children by their weights, plotting the results against the standard curve.

Ten tall boys were examined; 6 of them were 5 to 10 per cent too tall for their age, and 4, 10 to 20 per cent too tall (table 7). The results remain indubitably within normal limits (fig. 12 *A*). The fact that in this respect no difference was found between the boys less than 10 per cent

too tall and those with a greater deviation is in favor of the correctness of the method followed.

Among 14 short boys examined, 6 were 5 to 10 per cent and 7 were 10 to 20 per cent below standard height, and 1 was still smaller (table 8). Again all the results fall within normal limits, and no distinct difference is seen between the boys with smaller or greater deviation from the normal height. That all the points but 1 lie below the curve is of no importance, as the deviation from the standard curve is very small indeed (fig. 12 *B*).

Only 1 tall girl could be examined. Among the 31 small girls the proportions were as follows: 17 were 5 to 10 per cent too short, 11 were 10 to 20 per cent below average height and 3 were 20 to 30 per cent below. The results are shown in table 9. Here again the results are arranged on either side of the standard curve within the normal limits (fig. 13 *A*). The fact that an occasional point falls just outside is not surprising, as the number of determinations is rather high, and such deviations are often found in metabolic investigations, especially for girls.

Further evidence of the fact that age, as such, does not influence the basal metabolism is shown by observations on 2 abnormally small children, who were examined on repeated occasions with long intervals between (fig. 13 *B, C*).

Name	Date	Age		Weight, Kg.	Height, Cm.	Shortage in Height		Basal Metabolic Rate
		Yr.	Mo.			Cm.	Percentage	
M. P.	4/27/36	5	8	12.25	95	14	13	697 △
	6/26/37	6	10½	15.00	104	12	10	747 ▲

M. P., an extremely small girl who had a normal weight for her height, showed a normal basal metabolic rate as calculated by her weight. In fourteen months she grew at a normal rate, and the basal metabolic rate rose correspondingly. The other child, E. M., a genuine dwarf, grew but little in the two and a half years of observation. The deficiency in height increased from 16 to 21 per cent.

Name	Date	Age		Height, Cm.	Shortage in Height		Basal Metabolic Rate
		Yr.	Mo.		Cm.	Percentage	
E. M.	4/24/34	5	6	91.0	17.0	16	607 ○
	1/14/35	6	3	93.0	20.0	18	641 △
	10/ 2/35	7	..	94.0	22.5	19	646 ▲
	10/21/36	8	..	96.5	25.5	21	631 □

In spite of the fact that this girl had become two and a half years older, her basal metabolic rate, in accordance with her size, had remained practically the same.

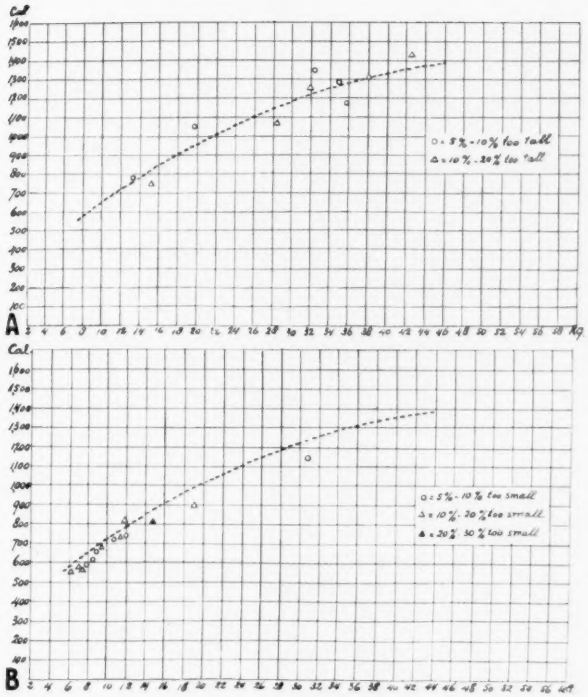

Fig. 12.—*A*, the basal metabolic rates of tall, well proportioned boys in calories per twenty-four hours referred to body weight. *B*, the basal metabolic rates of short, well proportioned boys in calories per twenty-four hours referred to body weight.

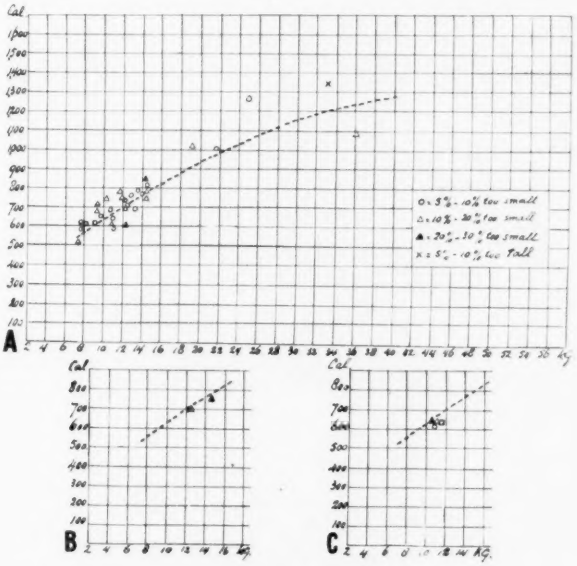

Fig. 13.—*A*, the basal metabolic rates of short, well proportioned girls and of 1 tall girl in calories per twenty-four hours referred to body weight. *B* (subject M. P.) and *C* (subject E. M.), basal metabolic rates of abnormally small children in calories per twenty-four hours referred to body weight.

Since in the present studies the 107 children investigated were divided into seven groups, the number in each group was too small to admit the drawing of positive conclusions concerning estimations of the basal metabolic rate. It was found, however, that for all groups the results pointed to the same conclusion. Therefore, I think it justifiable to accept the standards just postulated as provisionally valid for computing the basal metabolic rates of children with abnormal bodily dimensions. Meanwhile, further investigations on larger groups of children are desirable.

TABLE 9.—*Basal Metabolic Rates of Short Girls and of One Tall Girl*

Age		Height, Cm.	Weight, Kg.	Standard Height for Age	Shortage in Height			Basal Metabolic Rate, Calories per 24 Hours
Yr.	Mo.				Cm.	Percentage		
				A. Short Girls				
3	½	90.0	12.30	95.0	5.0	5		735
3	1	90.0	10.80	95.0	5.0	5		684
3	11	94.0	12.45	99.0	5.0	5		711
1	7½	77.0	9.70	82.0	5.0	6		652
2	4	84.0	11.00	89.0	5.0	6		641
2	11	88.0	13.25	94.0	6.0	6		692
4	8	97.5	14.50	104.0	6.5	6		815
1	5½	73.5	7.80	79.0	5.5	7		584
2	3½	80.5	11.15	87.0	6.5	7	○	591
3	3	89.0	13.50	96.0	7.0	7		791
6	10	108.0	21.60	116.0	8.0	7		1,006
1	5	72.5	7.70	79.0	6.5	8		618
2	6	83.0	9.10	90.0	7.0	8		616
4	7½	95.5	13.90	104.0	8.5	8		774
5	3½	98.5	12.90	106.5	8.0	8		761
10	..	122.0	24.90	132.0	10.0	8		1,262
1	7	75.0	8.15	82.0	7.0	9		614
4	6½	94.0	12.00	104.0	10.0	10		749
6	10½	104.0	14.50	116.0	12.0	10		747
7	2	105.0	19.05	117.0	12.0	10		1,012
5	8	95.0	12.25	109.0	14.0	13		697
3	1	82.0	9.40	95.0	13.0	14		682
6	1½	95.5	14.50	111.5	16.0	14	△	785
3	3	82.0	9.40	96.0	14.0	15		716
3	9	83.0	11.70	98.0	15.0	15		781
5	6	91.0	10.90	108.0	17.0	16		607
18	9	137.0	36.10	162.5	25.5	16		1,088
2	7½	74.0	10.15	91.0	17.0	19		746
Under 9	..	101.5	14.30	126.0	24.5	20		849
3	½	72.0	7.50	94.0	22.0	23	▲	517
6	11	85.0	12.30	116.0	31.0	27		603
				B. Tall Girl				
					Excess in Height			
10	4	144.0	33.20	132.0	12.0	+9	×	1,331

SUMMARY

For 120 normal boys and 123 normal girls whose body weights ranged from 6 to 46 Kg., the basal metabolic rates were estimated by means of the apparatus of Dusser de Barenne and Burger. On the basis of the figures obtained, standard curves for normal children were drawn up, the rates being calculated according to the weight.

By the same method the basal metabolic rates were determined for 107 children with abnormal bodily dimensions. The investigation concerned 13 fat boys, 22 fat girls, 6 thin boys and 10 thin girls. Besides,

measurements were done on 56 children who were too tall or too short for their age but otnerwise normally proportioned. These were divided as follows: 10 tall boys, 1 tall girl, 14 short boys and 31 short girls. With the aid of the results I have tried to draw up standards for determining the basal metabolic rates of children of abnormal size. The following mode of calculation is proposed:

1. For a fat boy with an excess of weight up to 35 per cent, the rate is based on the actual weight; with a greater excess of weight, on the standard weight for the actual height, increased by one third of the excess over the standard weight.

2. For a fat girl with an excess of weight up to 20 per cent, the rate is based on the actual weight; with a greater excess of weight, on the standard weight for the actual height, increased by one third of the excess over the standard weight.

3. For a thin boy or a thin girl, the rate is based on the actual weight.

4. For a well proportioned child who is too tall or too small for his age, the rate is based on the actual weight.

DENTAL DEFECTS IN CONGENITAL SYPHILIS

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Since Hutchinson (1859) [1] described the abnormality of the upper first permanent incisor which he believed to be the only dental defect reliably pathognomonic of congenital syphilis, considerable controversy has centered around the following questions: 1. Can the typical Hutchinsonian tooth be taken as a sign of congenital syphilis in all cases? 2. Can defects of the teeth other than those found in the upper first permanent incisor in cases of congenital syphilis also be considered as pathognomonic of this disease? 3. Can defects in the enamel occurring independently of or concurrently with congenital syphilis be clearly differentiated from the defects of syphilitic type?

The present communication concerns clinical observations on the developmental dental defects found in the permanent teeth of 8 patients with congenital syphilis. These patients, who had applied at the Outpatient Clinic of the Peiping Union Medical College Hospital for treatment during the years 1922 to 1927, were recalled and reexamined, and their hospital records were reviewed. Only those for whom a definite diagnosis of congenital syphilis had been established were included in this group. A review of the histories yielded no evidence of other diseases that were relevant to this study. The group comprised 3 male and 5 female patients whose ages ranged from 12 to 27 years. All were Chinese living in North China, and none had received antisyphilitic treatment either previous to or during the time that the affected teeth were developing. Other dental diseases, such as caries and periodontoclasia, had not significantly destroyed the evidence of the developmental defects of the teeth. Clinical descriptions, plaster models and photographs of the dental structures were made for the study.

A review of the findings showed that all of the 8 patients in this group had developmental dental defects. Undersized teeth were found in 7 of the group; the enamel coating was defective on the occlusal or incisal portion in 5; the enamel covering showed a smooth normal surface on gross examination in 1, and the upper incisors had grooved defects distributed in horizontal zones symmetrically over the labial aspect in another. All of these patients showed occlusal deformity.

From the Dental Study Unit, Yale University School of Medicine.

1. Hutchinson, J.: A Report on Malformations of the Teeth as Indicative of Diathesis, Tr. Path. Soc. London **10**:287, 1859.

Besides dental defects, corneal lesions were found in 4 of the 8 patients. One of these was active at the time examination was made. Two of these 4 patients with ocular lesions also had eighth nerve deafness.

According to Hutchinson's (1861) [2] earlier description, the typical malformed upper first permanent incisor of congenital syphilis is shorter and narrower than normal, with its mesial and distal sides converging from the gingival margin to the incisal edge. There is also a failure of development of the central mamillon, which causes the formation of a half-moon–shaped notch on the cutting edge of the tooth. The deficient enamel covering on the incisal edge permits staining of the underlying dentin, and consequently this portion of the tooth becomes darkened. In a later publication on the subject, Hutchinson (1887) [3] stated that he did not believe that the notching of the incisal edge was an essential part of a picture which was pathognomonic of congenital syphilis. Such a tooth might be shorter and narrower than normal, with the mesial and distal sides converging to meet an incisal edge having a slight defect in the enamel, which soon wore away. Hutchinson called this the screwdriver form.

Although Hutchinson (1876) [4] stated that other teeth were sometimes involved, he expressed the belief that only the affected first permanent incisor could be taken as pathognomonic of congenital syphilis.

A comparative description of normal and of syphilitic teeth was published by Moon (1884),[5] who pointed out that the first molars in congenital syphilis are "reduced in size and dome-shaped through the dwarfing of the central tubercle of each cusp" and that "syphilitic teeth may have a perfect covering of enamel and will not be discolored." He did not state, however, whether his observations were clinical or concerned extracted teeth. Roentgenograms were not available in his time.

Pflüger (1925)[6] reported a series of cases of congenital syphilis in which he noted defects of the first permanent molar which he considered typical of the disease. According to this investigator, the walls of the first molar crowns tapered from the cervical toward the occlusal surface

2. Hutchinson, J.: Hereditosyphilitic Struma, and on the Teeth as a Means of Diagnosis, Brit. M. J. **1**:515, 1861.

3. Hutchinson, J.: Syphilis: On Recognition of Inherited Taint, Philadelphia, Lea Brothers & Co., 1887, p. 431.

4. Hutchinson, J.: Constitutional Syphilis, in Reynolds, J. R.: A System of Medicine, ed. 3, London, Macmillan & Co., 1876, vol. 1.

5. Moon, H.: Dental Surgery, in Bryant, T.: A Manual for the Practice of Surgery, ed. 4, London, J. & A. Churchill, 1884, vol. 1, p. 637.

6. Pflüger, H.: Eine für Lues congenita characteristische Formveränderung (Knospenform) an dem ersten Molaren, München. med. Wchnschr. **71**:605, 1924.

and produced a bud-shaped tooth. Although he found this deformity in only 8 of the 56 cases, Pflüger expressed the opinion that the condition occurs more frequently but is obscured early in life owing to the ravages of dental caries.

The material used for the present study, as well as that of other workers, indicates that dental defects associated with congenital syphilis show wider variation than is generally known. This variation may range from complete failure of development of a tooth to slight diminution of size and alteration of form. The difference, however, is largely one of degree.

Photographs of the anterior regions of 3 sample sets of teeth from this group of patients with congenital syphilis may be seen in the figure, *A, B* and *C*. They are considered to have, respectively, slight, moderate and marked degrees of defect. The teeth of all members of the group had the general characteristics of those used as illustrations.

In *A* it is noted that the walls of the crowns of the maxillary first permanent incisors, in particular, converge toward the incisal edge. This deformity appears to be slightly imitated by the second incisors and cuspids. A defect in the enamel is seen on the labial aspect of the mandibular first incisor. No other clinical evidence of structural developmental defect of the enamel covering of the anterior teeth was found. Marked destruction by dental caries of 3 of the first permanent molars in this patient rendered these teeth useless for comparison. The occlusal surface of the 1 remaining maxillary first permanent molar presented a contracted appearance.

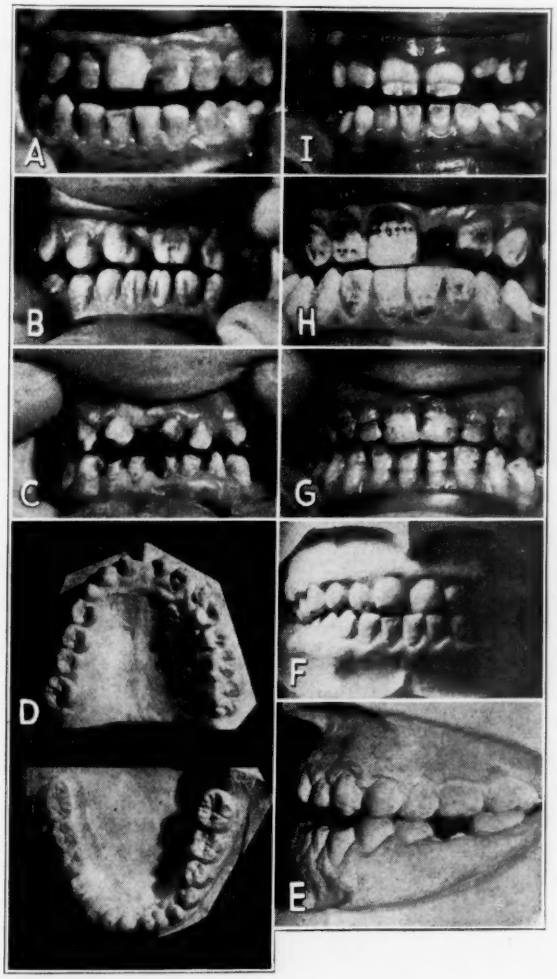
In *B* the left maxillary permanent cuspid is missing. All the other anterior teeth are malformed and undersized. The 4 first permanent incisors show evidence of failure of development of the central mamillons, but no other evidence of structural defect of the enamel is seen on gross examination. The 4 first permanent molars in this patient were all moderately undersized and malformed.

In *C* all of the permanent teeth except the third molars are present. The maxillary and mandibular incisors, cuspids and first molars are greatly reduced in size, show marked deformity and are wanting normal enamel covering.

D is a photograph of a plaster model giving another view of the teeth seen in *C*. The malformation and undersizing of the 4 first permanent molars is clearly shown. Although the defect seen in this illustration is marked, the tendency toward this condition was present in all of the members of the group.

E illustrates a peculiar open bite deformity observed in this group. The model was made from the teeth of a patient 19 years of age. The open bite seen in this illustration is the most pronounced found, but the

tendency toward the condition was observed in 6 of the 8 members of the group. Although the teeth seen in *A, B* and *C* are being held apart slightly in order to afford a better view of the outline of the incisal edges, those seen in figure *C* remained open, and those in *A* and *B* came into edge to edge contact when the teeth were in centric occlusion *(F)*.



Photographs illustrating characteristic dental defects. In *A, B* and *C* are seen the anterior regions of dental structures with defects of slight, moderate and marked degree, respectively. *D* shows a plaster model of the teeth seen in *C*. *E* and *F* picture plaster models which show the open bite deformity. *G, H* and *I* illustrate defects associated with rickets.

In comparing this type of open bite with those associated with habits such as thumb sucking, with crowding in the anterior region owing to

inadequate development of the arch or with failure of proper eruption of the teeth, certain differences are clearly observed. The open bite of congenital syphilis shows no contraction of the anterior region such as produces crowding of the teeth; there is not the bent or distorted appearance of the alveolar process seen in the open bite resulting from habits, nor is there evidence of failure of proper dental eruption. In the open bite associated with congenital syphilis the teeth, as well as their supporting bony structures, appear to be wanting in sufficient substance to bring them into proper occlusal relations. The malocclusal deformity observed in this group apparently corresponds to that described by Chompret (1900).[7] He did not state the frequency of occurrence or ascribe to it important diagnostic significance. The regional bony changes which Bauer (1931)[8] found in cases of congenital syphilis may be an important factor in the production of the open bite deformity.

Of the various types of developmental dental defects encountered clinically, that of rickets is one which is not always easily differentiated from that of congenital syphilis. *G*, *H* and *I* are photographs, approximately of actual size, of defective teeth associated with rickets. *I* illustrates the condition manifesting itself in the incisal and occlusal region of the teeth; *H* suggests that the damage was done after the incisal and occlusal but before the cervical portions of the teeth were calcified, and *G* shows the zonal and symmetric distribution of the defect over the surfaces of the teeth.

The same groups of teeth are commonly affected both in cases of congenital syphilis and in cases of rickets. With congenital syphilis a tooth on one side of the jaw may be affected when the corresponding one on the opposite side is not, or there may be a greater degree of damage on one side. There is not the marked symmetric distribution over the teeth that is associated with rickets, nor is the defect limited to certain zones on the crown of the tooth. With rickets only those portions of the teeth that are calcifying at the time the disease is active are affected (Eliot and others, 1934).[9] The other portions attain their normal size and form regardless of the severity of the disease. With congenital syphilis teeth are malformed and diminished in size, and there may be a failure of enamel, particularly of the mamillons and cusps. One of the most striking features of this defect of the enamel is the failure of the central mamillon, described by Hutchinson. If the involved zone of the defect associated with rickets is in the incisal and occlusal regions, it

7. Chompret, M.: Malformations buccales dans l'heredo-syphilis, Compt. rend. Cong. internat. de med., Paris (Sect. Stomatol.), 1900, p. 148.

8. Bauer, W.: Ueber Befunde am Zahnkeim und Kieferknochen bei angeborener Syphilis, Wien. klin. Wchnschr. **44**:879, 1931.

9. Eliot, M. M.; Souther, S. P.; Anderson, B. G., and Arnim, S. S.: Study of the Teeth of a Group of School Children Previously Examined for Rickets, Am. J. Dis. Child. **48**:713 (Oct.) 1934.

is not so clearly differentiated clinically from the defect typical of congenital syphilis. It is conceivable that both types of defect may appear concurrently or that the failure of calcification in both instances is owing to associated hypocalcemia. Fleischmann (1908) [10] suggested that hypoplasia of the enamel was probably always the result of tetany or of latent tetany. The fundamental differences in the two diseases themselves should not be overlooked. Rickets is a generalized deficiency disease involving the calcium-phosphorus metabolism, while syphilis is a generalized infection that tends to be more localized than rickets.

The concurrence of eighth nerve deafness, interstitial keratitis and defects of the first permanent maxillary incisors in cases of congenital syphilis, known as Hutchinson's triad, has been questioned. In contrast to earlier observers, most of the more recent writers agree that this is of rare occurrence. Stathers and Skidmore (1932)[11] found it to be present in only 1 of 105 cases. If one disregards the typical deformity of the central incisor alone, which Hutchinson believed to be the only reliable dental diagnostic sign of congenital syphilis, and considers that such defects as are here presented are also typical of the disease, the triad is then observed to have been present in 2 of the 8 patients included in this group. It is reasonable to expect to find it more frequently in groups of persons with untreated syphilis, since under such conditions the eighth nerve deafness and interstitial keratitis are permitted to develop.

SUMMARY

The dental abnormalities having the characteristics described in the report are considered to be of congenital syphilitic origin. An attempt is made to view the dental structure as a whole and to observe what portions of it or what groups of teeth are involved rather than to give minute, detailed descriptions of individual teeth that may be diagnostic of congenital syphilis. When examined in this manner, the dental defects associated with congenital syphilis stand out more clearly. In each of the patients the 8 incisors, 4 cuspids and 4 permanent molars were involved whenever they were present.

The most characteristic features of the abnormality seen clinically were (1) the undersized, malformed appearance of the teeth, (2) the contracted appearance of the mamillons, marginal ridges and cusps of the incisors, cuspids and molars and (3) a peculiar open bite malocclusion.

Defects of the eyes, ears and teeth were found in 2 of the 8 patients with congenital syphilis which was untreated during the period of development of the affected teeth.

10. Fleischmann, L.: Beziehungen zwischen der Tetanie und der Entwicklung von Defektbildungen des Zahnschmelzes, Mitt. d. Gesellsch. f. inn. Med. u. Kinderh. **7**:182, 1908.

11. Stathers, F. R., and Skidmore, R. M.: Asymmetrical Dental Stigmata in Congenital Syphilis, J. Dent. Research **12**:441, 1932.

ARTERIAL OXYGEN SATURATION AND EFFECT OF OXYGEN THERAPY IN PULMONARY DISEASES

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In many cases, the arterial oxygen saturation will decrease with disease of the lung. The decrease may be caused by various factors: 1. Diminished ventilation may result from (*a*) stenosis of the air passages, e. g., stenosis of the larynx and bronchi due to inflammatory processes; (*b*) a decreased movement of the thoracic wall caused by weakness of the respiratory muscles, as with rickets and (*c*) a decreased function of the central nervous regulation, often found in very young children. The consequence of this disturbance of ventilation is diminution of the alveolar oxygen tension. Under these conditions the blood cannot take up sufficient oxygen, and the arterial oxygen saturation decreases (hypoxic hypoxemia).

2. There may be decreased diffusion into the pulmonary capillaries. This occurs if the alveolar epithelium is swollen or covered by exudate.

Seriously lessened saturation may result if considerable circulation is maintained through parts in which the oxygen uptake is defective. Conditions will be bettered by the obstruction of the circulation in the affected parts. The blood will then pass through the normal portions, where it will take up sufficient oxygen. If the area of circulation becomes too small, the contact of the blood with the alveolar air will become too much restricted, and therefore unsaturation will occur. If the alveolar oxygen tension falls, the oxygen tension and the saturation of the arterial blood will decrease in consequence.

When even a small rise in the carbon dioxide tension of the blood stimulates the respiratory center, a fall of the oxygen tension has considerably less influence. A greater fall of the arterial oxygen tension may produce the contrary effect, the central nervous tissues being extremely sensitive to lack of oxygen. When the hypoxemia has reached a certain degree, the irritability of the respiratory center may decrease, with respiration becoming more shallow. Thus a vicious circle is formed: insufficient ventilation, hypoxemia, injury of the respiratory center and shallow and irregular breathing, which causes an increase of the hypoxemia. This vicious circle can be broken by the administration of oxygen or of drugs which excite the respiratory center, or by physical stimuli which deepen the ventilation.

From the Pediatric Clinic; Director, Prof. Dr. J. van Lookeren Campagne.

Hypoxemia is not necessarily associated with marked cyanosis. The occurrence of cyanosis depends on the absolute amount of reduced hemoglobin in the capillaries. In cases of anemia there is a small quantity of reduced hemoglobin, even with marked hypoxemia, and cyanosis is not detected. On the other hand, the reduced blood can stagnate in the capillaries and the smallest veins of the skin. In this case there is a cutaneous stagnant type of hypoxemia, with normal oxygen saturation in the arterial blood.

To ascertain the degree of hypoxemia one must determine the oxygen saturation of the arterial blood.

The arterial oxygen saturation is relatively seldom determined under clinical conditions. The Van Slyke method requires so much blood that an arterial puncture has to be made. The advantage of the microdeterminations is that they can be done on amounts of blood which can be taken easily from a hyperemized capillary area.

In such an area the flow of blood is so accelerated that the oxygen saturation of the capillary blood is the same as that of the arterial blood. This has been shown by various authors.[1]

For a control test I determined the oxygen saturation of the blood taken from a hyperemized capillary area for 28 healthy children ranging in age from 2 months to 12 years. In all cases values normal for the arterial oxygen saturation were found (91 to 98 per cent).

In a person breathing pure oxygen the oxygen saturation, as determined by the micromethod, increased to 100 per cent. It follows that if the oxygen saturation of the capillary blood of a hyperemized area is not the same as that of the arterial blood, the former will not rise to 100 per cent.

Till now the available microdeterminations have not found clinical application. Brinkman and Wildschut [2] and Brinkman and I [3] have described two colorimetric methods which can be used under clinical conditions. By these methods it is possible to determine quickly the oxygen saturation of 0.5 cc. of blood.

Both methods are founded on the difference in absorption of light of special wavelength by hemoglobin and by oxyhemoglobin. While Brinkman makes use of the neon lamp and measures the absorption of the light by a photo element, I use as a source of light the blue line of the mercury spectrum and determine the absorption with a good photometer.

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1. Verzár, F., and Keller, F.: Biochem. Ztschr. **141**:21, 1923. Lundsgaard, C., and Möller, E.: J. Exper. Med. **36**:559, 1922. Goldschmidt, S., and Light, A. B.: J. Biol. Chem. **64**:53, 1925.

2. Brinkman, R., and Wildschut, A. J. H.: Acta med. Scandinav. **94**:459, 1938.

3. Brinkman, R., and Jonxis, J. H. P.: Acta med. Scandinav. **94**:453, 1938. Jonxis, J. H. P.: ibid. **94**:467, 1938.

PRINCIPLE OF THE COLORIMETIC METHOD

In the red as well as in the blue part of the spectrum there is a considerable difference in absorption of light by solutions of hemoglobin and of oxyhemoglobin. According to Beer's law, the concentrations of solutions of pure hemoglobin as well as of solutions of oxyhemoglobin are proportional to the logarithm of the transmitted light. The same applies to mixtures of hemoglobin and oxyhemoglobin.

One can determine in these mixtures the percentage of oxygenated and of reduced hemoglobin from the quantity of light absorbed by the sample in the original, in the completely reduced and in the oxygenated condition (fig. 1). On the abscissa the concentrations of hemoglobin in grams per hundred cubic centimeters are plotted; on the ordinate the extinction (2 minus the logarithm of the percentage of absorbed light) is set out. The lines *AB* and *AC* give the absorption of light (mercury vapor lamp, Zeiss filter Hg 436) by hemoglobin and by oxyhemoglobin, respectively. From figure 1 it may be deduced that for a given concentration of hemoglobin the quotient of the extinction values for the reduced and the oxygenated states amounts to 2.95. *D* indicates the absorption by a

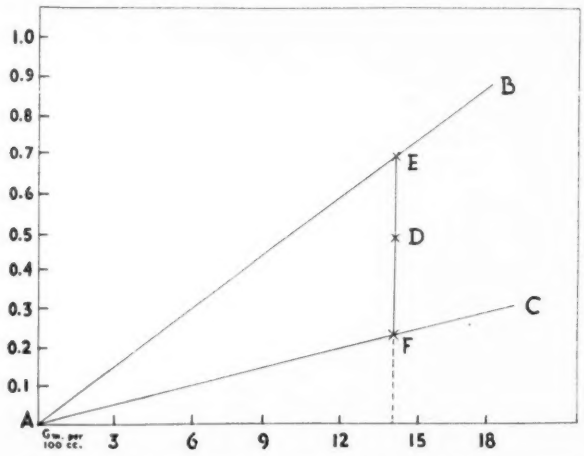

Fig. 1.—Chart showing absorption of light by hemoglobin and by oxyhemoglobin in the original, the completely reduced and the oxygenated condition. On the abscissa the concentrations of hemoglobin (grams per hundred cubic centimeters) are plotted; on the ordinate the extinction (2 minus the logarithm of the percentage of absorbed light) is set out. *AB* and *AC* indicate the absorption of light by hemoglobin and by oxyhemoglobin, respectively. *D* indicates the absorption by a mixture containing 14 Gm. of hemoglobin and oxyhemoglobin. *E* and *F* indicate the extinction by a solution of hemoglobin and one of oxyhemoglobin, respectively.

mixture containing 14 Gm. of the two pigments, hemoglobin and oxyhemoglobin. *E* and *F*, respectively, indicate the extinction by a solution of hemoglobin and of oxyhemoglobin in the same concentration.

If one measures the absorption of the original blood and of the same blood in the reduced state, one can calculate the extinction of oxygenated blood from the extinction of the fully reduced sample by dividing the first value by 2.95. Thus if the extinction of the original blood is found to be 0.70, and that of the

same blood in the fully reduced state, 1.80, the percentage of oxygenated hemoglobin will be $\frac{(1.80 - 0.70) \times 100}{1.80 - \frac{1.80}{2.95}}$. The factor 2.95 is independent of the concentration but changes with the wavelength of the light used. The values found by this method are exactly the same as those obtained by the Van Slyke manometric method.

TECHNIC OF THE COLORIMETRIC METHOD

The arterial blood can be taken by puncturing the heel with a vaccinostyle, the heel having been kept for five minutes in water of 48 C. Since the heating causes local arterial hyperemia, the capillary blood may be considered as purely arterial. Only with severe disturbance of the venous return will the capillary blood not be purely arterial, in spite of the intensive flow of blood. However, the arterial flow can be restored temporarily by elevation and massage of the member, so that even with such a disturbance this method of taking the sample of blood may be used without too great errors. The blood must be taken under liquid petrolatum without contact with air. For this purpose a small glass vessel with a pointed bottom is completely filled with liquid petrolatum and held directly against the wound. Before coagulation occurs the blood is drawn up into a small, well closed syringe (contents 0.5 cc.). The dead space of the syringe has previously been filled with a concentrated solution of saponin. The blood in the syringe is mixed with this solution, so that hemolysis occurs. To facilitate mixing a small gold globule is placed in the syringe. A drop of this hemolyzed blood is put into a container so quickly that there is the least possible contact with air. As a container we prefer a blood cell counting chamber (without grating) 0.01 mm. high. As the height is exceedingly small, there is so little contact with air that the absorption of oxygen occurs very slowly. The rest of the hemolyzed blood in the syringe is completely reduced by stirring with some crystals of sodium hydrosulphite. A drop of this blood is also brought into a container 0.01 mm. in height. If the estimation cannot be made at once, one may store the contents of the syringe in a narrow tube under liquid petrolatum for some hours in a dark place at a freezing temperature.

In this manner the oxygen saturation of the arterial blood was examined for a number of children. For 28 healthy children ranging in age from 2 months to 12 years, normal values were found for the arterial oxygen saturation (about 97 per cent). For those with various pulmonary diseases, the values were entirely different.

LOBAR PNEUMONIA

I determined the oxygen saturation in 10 cases of lobar pneumonia.

In these cases of uncomplicated lobar pneumonia there was normal or slightly decreased oxygen saturation of the arterial blood. As it is not probable that diffusion of oxygen occurs freely in the affected parts of the lung, the slight decrease in the arterial oxygen saturation shows that in the affected parts the circulation as well as the ventilation must be greatly hindered. The greater part of the blood passes through the normal portions of the lung and there can take up sufficient oxygen. In

these patients oxygen therapy would not have had any effect, even though cyanosis was noted in case 3. Obviously this cyanosis must have been caused by venous retardation and not by deficient uptake of oxygen

TABLE 1—*Cases of Lobar Pneumonia in Which Oxygen Saturation Was Normal or Slightly Decreased*

Case No.	Age, Yr.	Oxygen Saturation, Percentage	Clinical Data
1	4	90	Lobar pneumonia of upper lobe of left lung; disease had normal course; determination made on fourth day of illness, before crisis; cyanosis not present
2	6	91	Lobar pneumonia of lower lobe of right lung, no complications; determination made on fifth day of illness, before crisis; cyanosis not noted
3	7	88	Lobar pneumonia of middle and lower lobes of right lung; disease had normal course; determination made on seventh day of illness, just before crisis; at that moment slight cyanosis noted
4	8	94	Central lobar pneumonia; disease had normal course; determination made shortly before crisis, on seventh day of illness

TABLE 2.—*Cases of Lobar Pneumonia in Which Oxygen Unsaturation Disappeared Before the Crisis*

Case No.	Age, Yr.	Oxygen Saturation, Percentage		Clinical Data
		First Test	Test Made 2 Days Later	
6	3	65	88	Lobar pneumonia of right lung without complication; when admitted on third day of illness patient had marked cyanosis, which disappeared before crisis
7	5	73	95	Lobar pneumonia of right lung without complication; when admitted on third day of illness patient had marked cyanosis which soon disappeared

TABLE 3.—*Cases of Lobar Pneumonia in Which Marked Increase in Oxygen Saturation Followed Administration of Oxygen*

Case No.	Age, Yr.		Oxygen Saturation, Percentage	Clinical Data
8	4		69	Extensive lobar pneumonia of left lung; admitted on fifth day of illness with marked cyanosis; after administration of oxygen arterial oxygen saturation increased to 88%; determination made on sixth day of illness
9	6	On fifth day of illness	70	Extensive lobar pneumonia of right lung, pneumococcus type I; marked cyanosis; child appeared gravely ill
		On sixth day of illness	75	
		On eighth day of illness	88	
		On sixteenth day of illness	95	
10	7		64	Extensive lobar pneumonia of right lung; determination made on fifth day of illness; marked cyanosis; after administration of oxygen, oxygen saturation increased to 89%

in the lung. It was of the stagnant type. While in the fully developed stage of lobar pneumonia the arterial unsaturation hardly decreased, in the incipient stage there was found oxygen saturation, which disappeared before the crisis. It was probably due to the fact that at first ventilation or diffusion is defective, while later the corresponding circulation is

decreased. During the first days considerable amounts of blood pass through the involved parts but cannot take up sufficient oxygen, so that the oxygen saturation begins to decrease.

When large areas of the lung are involved, the large amounts of blood will have to flow through the normal parts. Here the capillaries

TABLE 4.—*Cases of Bronchopneumonia in Which Oxygen Saturation Improved After Oxygen Therapy*

Case No.	Age	Oxygen Saturation, Percentage: Before Oxygen Therapy	Oxygen Saturation, Percentage: After Oxygen Therapy	Clinical Data
11	3 months	30	72	Extensive bronchopneumonia of both lungs; moderate cyanosis; hemoglobin 48%
	1 day later	42		
	2 days later	32		
	14 days later	74		
12	8 months	30	97	Extensive bronchopneumonia of both lungs after whooping cough; moderate cyanosis; hemoglobin 51%
	1 day later	68		
	6 days later	59		
	7 days later	60		
	14 days later	82		
	23 days later	74		
	30 days later	94		
13	5 months	64	..	Bronchopneumonia of both lungs after whooping cough; slight cyanosis; hemoglobin 45%
14	1 year	83	..	Bronchopneumonia after whooping cough
15	1 year	88	..	Bronchopneumonia, especially of right lung
16	1 year	80	..	Bronchopneumonia of right lung
17	1 year	86	..	Bronchopneumonia of right lung
18	1 year	60	..	Bronchopneumonia of both lungs; no cyanosis; hemoglobin 46%
19	1 year	84	..	Bronchopneumonia of both lungs
20	2 years	63	..	Bronchopneumonia, especially of right lung, after whooping cough; slight cyanosis; hemoglobin 46%
21	2 years	77	..	Bronchopneumonia of both lungs
22	2 years	73	99	Bronchopneumonia of both lungs; slight cyanosis
23	2 years	86	..	Bronchitis with some localized bronchopneumonia areas
24	2 years	65	92	Extensive bronchopneumonia; moderate cyanosis

will become overfilled, so that the contact of the blood with the alveoli will become less intensive. Owing to this the saturation is diminished.

In cases 8 and 10 one can notice the marked influence of the administration of oxygen. In spite of the decreased contact of the blood in the overfilled lung capillaries, in these circumstances the blood can take up sufficient oxygen in the unaffected parts by the rise in the alveolar oxygen tension.

BRONCHOPNEUMONIA

In all cases of bronchopneumonia in which tests were made, a decrease of the arterial oxygen saturation was found. This can be explained by the fact that various sections of the lung are badly ven-

tilated. In infants the unsaturation is more pronounced. This is probably due to the fact that even in a normal baby the respiration is relatively shallow. In infants the alveolar oxygen tension will decrease with slight obstruction of the air passages.

In cases 11, 12, 22 and 24, in which tests were made, oxygen therapy produced a distinct improvement. In most cases the oxygen saturation could be brought up to normal.

At a continuous saturation of 30 per cent, which I found in cases 11 and 12, life is not possible for adults. It is true that these infants were gravely ill, but they were not in a dying condition. Both children recovered. It may be assumed that the infant has better resistance to

TABLE 5.—*Cases of Tuberculosis in Which There Was Slight Decrease in Oxygen Saturation*

Case No.	Age	Oxygen Saturation, Percentage	Clinical Data
25	2 years	75	Tuberculous infiltration on right; greatly enlarged hilus, which compressed right main bronchus
26	1 year	80	Tuberculous infiltration on right; spontaneous pneumothorax on left
27	1 year	84	Tuberculous infiltration on left
28	7 years	86	Tuberculous infiltration on left
29	10 years	86	Tuberculous pleuritis with moderate exudate on left
30	3 years	90	Extensive epituberculous infiltration on right
31	8 years	92	Extensive tuberculous infiltration on right
32	10 years	95	Small tuberculous infiltration of right hilus
33	2 years	95	Tuberculous infiltration on left
34	2 years	96	Tuberculous peribilar infiltration on both sides
35	2 years	97	Primary complex on right
36	5 months	97	Small tuberculous peribilar infiltration on left

such severe anoxemia than the adult. This is indicated by the values found by Haselhorst and Stromberger [4] and by Noguchi [5] for the oxygen saturation of the fetal blood and by my unpublished data on the blood of prematurely born children.

If one correlates the occurrence of clinical cyanosis with the values of arterial saturation, it appears that cyanosis is not a good indication for the presence of arterial anoxemia. In many cases there is anemia, which prevents the occurrence of cyanosis (cases 11, 12, 13, 18, 20).

In a further study I was able to determine the arterial oxygen saturation of patients with pulmonary tuberculosis. In most cases the divergences from normal values were slight, even with rather extensive involvement. This might signify that there is a poor flow of blood through the affected parts, the remaining portions taking over their

4. Haselhorst, G., and Stromberger, K.: Ztschr. f. Geburtsh. u. Gynäk. **100**: 48, 1931.

5. Noguchi, M.: Jap. J. Obst. & Gynec. **20**:218, 1937.

function. When, however, ventilation is hindered by the compression of the bronchial tree due to a swollen gland, the oxygen saturation decreases (case 25).

TUBERCULOSIS

When large parts of the lung are affected, as with caseous pneumonia and miliary tuberculosis, there is a considerable decrease of the arterial oxygen saturation.

In case 41 the venous oxygen saturation was considerably lower (15 per cent). The oxygen consumption in the tissues may have been about normal. The oxygen tension in the blood, however, would have

TABLE 6.—*Cases of Tuberculosis in Which There Was Considerable Decrease in Oxygen Saturation*

Case No.	Age	Oxygen Saturation, Percentage: Before Oxygen Therapy	Oxygen Saturation, Percentage: After Oxygen Therapy	Clinical Data
37	2 years	77	80	Caseous tuberculosis; bronchopneumonia
	1 day later	80		
	2 days later	90		
	7 days later	55		
	9 days later	50		
38	1 year	87	..	Miliary tuberculosis
	1 day later	78		
39	8 months	68	..	Miliary tuberculosis
40	7 years	43	84	Miliary tuberculosis, 24 hours before death
41	7 years	40	68	Exudative miliary tuberculosis; marked cyanosis; at autopsy, lung tissues almost completely filled with gelatinous masses; alveoli filled with air only in small portions of lungs
	1 day later	60	83	
	4 days later	39		
	7 days later	43		
	9 days later	56		

to decrease to extremely low values to make such utilization of oxygen possible. It is not conceivable that life is possible with such low oxygen tension in the plasma. Notwithstanding the low oxygen saturation, the oxygen tension appeared to be higher than could be expected from a normal dissociation curve (fig. 2). The dissociation curve was experimentally shown to be shifted to the right. This alteration in the dissociation curve was caused here by changed properties of the hemoglobin.[6]

These patients suffering from severe tuberculous processes with arterial oxygen unsaturation will respond to administration of oxygen, but less easily and less completely than those with bronchopneumonia. This may be explained by the fact that there is diminished diffusion of oxygen through the affected tissues.

OXYGEN TENT

In oxygen therapy for young children I use a new model of oxygen tent (fig. 3).

6. Jonxis, J. H. P.: Maandschr. v. kindergeneesk. **7**:58, 1937.

A cylinder of uninflammable celluloid is closed at the upper end by a tin plate with cooling ribs. At the top of these ribs is an opening for the inflow of oxygen. On the other end of the cylinder an airproof sheet is tightly fastened. The sheet forms a cylinder. At the upper end it has shoulders for giving better accommodation to the child. The whole outfit is put into the bed of the patient, with a little pillow in the celluloid cylinder. In the sheet are some trays filled with soda lime for binding the carbon dioxide. The child is put into the tent, his head being placed in the celluloid cylinder. The lower end of the sheet is tied up. As there

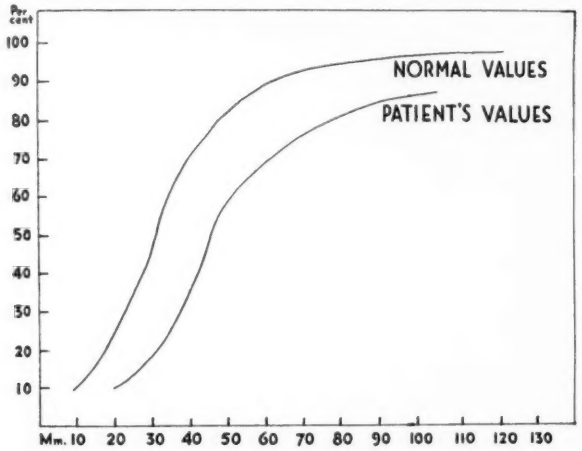

Fig. 2.—Dissociation curves of a normal subject and a patient with miliary tuberculosis (case 41). The abscissa indicates oxygen tension in millimeters of mercury, and the ordinate, the percentage of saturation of mercury with oxygen.

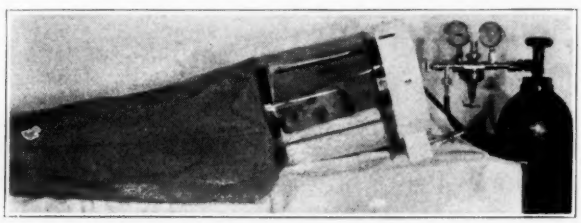

Fig. 3.—The oxygen tent in use.

is very little leakage, slight hypertension occurs, which brings about inflation of the tent. As soon as the tent has become rounded, the oxygen inflow is diminished to 2 liters a minute; this prevents decrease of the oxygen concentration in the tent. The water vapor condenses on the cooling ribs, which also take up the superfluous heat; they are cooled by an ice tank at the back of the ribs. If pure oxygen were used, the oxygen concentration would rise to more than 70 per cent. As such a degree of concentration might be harmful, I use a mixture of 80 per cent oxygen and 20 per cent nitrogen. With a flow of 2 liters per minute the mixture in the tent consists of about 60 per cent oxygen and 40 per cent nitrogen, the concentration of carbon dioxide not rising above 1 per cent.

The advantages of this tent are (1) economical use of oxygen; (2) an extremely small amount of leakage, which prevents decrease of the oxygen percentage in the tent, and (3) possibility of rapid increase of the oxygen concentration (in five minutes) to 60 per cent. This is important, as the tent often has to be opened for nursing, which always causes a considerable fall in concentration.

SUMMARY

1. A method for the determination of the arterial oxygen saturation in clinical conditions is described.

2. The arterial saturation found in cases of lobar pneumonia, bronchopneumonia and pulmonary tuberculosis is reported, and the influence of the oxygen therapy is pointed out.

3. An oxygen tent for children is described.

CONCLUSIONS

1. In cases of pulmonary disease, the arterial oxygen saturation is a better indicator of the degree of the arterial hypoxemia than cyanosis is.

2. By means of determining the arterial oxygen saturation the need for oxygen therapy can be better shown and the effect of this treatment can be better followed.

3. With lobar pneumonia, at least during full development of the disease, there is slight oxygen unsaturation in the cases in which there are no complications.

4. However, when large portions of the lung are affected the unsaturation may increase.

5. In most cases of bronchopneumonia there is considerable unsaturation.

6. With bronchopneumonia this decrease seems to be most pronounced in infants.

7. With bronchopneumonia as well as with lobar pneumonia oxygen therapy is effective against arterial unsaturation.

8. Various forms of pulmonary tuberculosis may cause unsaturation.

TIME AND STAGE IN DEVELOPMENT AT WHICH FACTORS OPERATE TO PRODUCE MONGOLISM

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In general, it is obvious that the factor or factors that bear a direct causal relationship to a condition which is clearly apparent at the time of birth—as, according to Brousseau,[1] is the case with mongolism—must operate at the time of the formation of the gametic chromosomes or subsequently, during the development of the embryo but before the time of delivery. It is believed that a knowledge of the exact time at which such factors operate would markedly facilitate progress toward an understanding of the etiology of such a condition.

HEREDITARY FACTORS

If the condition is produced by genetic factors, then it should be possible to demonstrate among closely related persons who bear any given trait specific relationship configurations that would be diagnostically characteristic of such hereditary factors. The simplest and most definite of these are the various but well known forms of simple mendelian inheritance. But when clearcut data directly indicative of some such simple mode of inheritance are not apparent, as Macklin [2] has shown to be the case with mongolism, the incidence method that has been used so successfully by Davenport [3] and others in demonstrating the hereditary nature of twinning is probably the most direct and useful. This method involves the comparison of the incidence of a trait among the groups of persons who are most closely related to a person bearing this trait with the incidence of the trait in the general population or, more specifically, in the part of the population within which the affected persons first appeared.

From Letchworth Village.

1. Brousseau, K.: Mongolism, Baltimore, Williams & Wilkins Company, 1928.

2. Macklin, M. T.: Mongolian Idiocy: The Manner of Its Inheritance, Am. J. M. Sc. **178**:315-337 (Sept.) 1929.

3. Davenport, C. B.: Influence of the Male in the Production of Human Twins, Am. Naturalist **54**:122-129, 1920; Heredity of Twin Births, Proc. Soc. Exper. Biol. & Med. **27**:75-77, 1920; Influence of the Male on the Production of Twins, M. Rec. **97**:509 (March) 1920; Does the Male Have an Influence in Human Twin Production? Ztschr. f. indukt. Abstammungs- u. Vererbungslehre **46**:85-86, 1927.

With a trait that has a fairly high incidence in the general population, this method is most useful, for it is but necessary to examine the 90 or 100 persons who are most closely related to each of the affected persons in order to determine the incidence of the trait in such a group. If no statistically significant occurrences of other affected persons appears in such a group, one may conclude that the trait is nonhereditary. On the other hand, the statistically significant occurrence of one or more affected persons indicates that the trait may be hereditary. If the incidence in such a group is markedly higher than it is in the general population, the size of the group is correspondingly reduced. Sometimes, as shown by Davenport [3] and others in the case of twinning, the incidence may be approximately 8 to 10 per cent; in such cases the reduction in the size of the group is marked.

On the other hand, the conclusive and positive demonstration that a rare trait is nonhereditary requires an examination of a correspondingly large group of persons, while in case of some of the extremely rare traits the groups become so large as to make the application of the incidence method utterly impracticable. In lieu of evidence to the contrary, the trait in such a case must be tentatively considered as nonhereditary.

It is difficult to obtain reliably accurate figures for the incidence of such a condition as mongolism in the general population; for even though, according to Brousseau [1] and others, this condition can generally be recognized at the time of birth, the literature contains few references to observations based on diagnoses that were included in the general routine observations required for the birth records of hospitals. When these observations have been made, however, it is probable that they provide the most reliable figures that can be obtained for the incidence of the condition, for in such cases the diagnoses are made by specialists at a time when a high infant mortality cannot have operated markedly to alter the results. So far as is known, however, the only direct determination of the incidence of mongolism based on the birth records of a hospital is that provided by Jenkins.[4] He found that among the 3,818 infants born in the Presbyterian Hospital, Chicago, during the years from 1926 to 1931 inclusive, there were 6 with mongolism, which gave a ratio of 1:636, or 0.16 per cent. The small number of births considered, however, renders this determination unreliable.

Determinations based on the occurrence of mongolism in the outpatient clinics are subject to errors from two sources. First, the ages of the children treated allow time for the mortality rate (well known

4. Jenkins, R. L.: Etiology of Mongolism, Am. J. Dis. Child. **45**:506-519 (March) 1933.

to be high among those with mongolism, as shown by Bleyer [5] and others) to operate in a way such as to reduce the value of the incidence. Second, since the figure for the general population does not include the children who remain well but who would nevertheless have visited the clinic if they had had need of medical care, the value of the incidence is somewhat increased.

With these factors clearly in mind, one may consider the values that Bleyer [5] obtained from the outpatient department of the St. Louis Children's Hospital and the Washington University School of Medicine. He found that among 47,923 children, ranging in age from 2 weeks to 14 years, there were 115 with mongolism, the ratio being approximately 1:417, or 0.24 per cent. On further analysis of his data, Bleyer found that the ratio for the occurrence of mongolism in children 3 years of age and under was 1:275, whereas the ratio for the children between the ages of 4 and 14 was 1:650.

This high mortality of persons with mongolism during the early years of life tends markedly to reduce the values for the incidence of the condition which are based on the number of cases that occur in an institution as compared with those in the population of the area from which the patients come. If to this factor is added the condition that economic and other environmental circumstances of the families in which mongolism occurs play an exceedingly important role in determining, among all the persons with mongolism in a certain area, how many and which ones are to be institutionalized, it is probable that figures determined on such a basis will be still further reduced. Further owing to the fact that those afflicted are generally affectionate, good-natured persons whose care is not difficult in comparison with that of many who have other forms of mental deficiency, it is difficult to locate in any general population all the persons with mongolism who are not institutionalized.

These may be, in part at least, the reasons for the low incidence for mongolism found by Doxiades and Portius. [6] In a rural population of 75,274 persons he found 11 instances of mongolism, an incidence of 1:6,843, or 0.014 per cent; while in an urban population of 340,157 he obtained 47 cases, an incidence of 1:7,237, 0.013 per cent. Von der Scheer, quoted by Doxiades and Portius,[6] obtained an incidence of 1:1,000, or 0.1 per cent, for institutionalized persons with mongolism from the population of a single German province.

5. Bleyer, A.: The Frequency of Mongoloid Imbecility, Am. J. Dis. Child. **44**:503-508 (Sept.) 1932.

6. Doxiades, L., and Portius, W.: Zur Aetiologie des Mongolismus unter besonderer Berücksichtigung der Sippenbefunde, Ztschr. f. menschl. Vererb.- u. Konstitutionslehre **21**:384-446 (Jan.) 1938.

These factors too must be carefully considered when one evaluates the figures provided by numerous workers for the incidence of mongolism in the group comprising all forms of feeblemindedness. These figures may vary, as stated by Doxiades and Portius,[6] Brousseau [1] and numerous other authors, from 1.23 per cent, given by Bourneville for France, to between 15 and 25 per cent, given by Hellsten for Russia.

In view of the absence of sufficient significant data on which to base a reliable determination of the incidence of mongolism, it is impossible to establish the number of persons most closely related to those with this condition concerning whom one must obtain information before one can make a positive statement relative to the role of heredity in the production of mongolism. For these reasons, it is impossible to state a final conclusion in regard to hereditary factors in mongolism. The marked infrequency of the occurrence of more than 1 case of mongolism in a family is, however, significant; for according to Doxiades and Portius [6] there are in all of the literature descriptions of only 50 such occurrences, while Macklin [2] found among 2,491 families but 30. In view of the large number of cases of mongolism that are known, this number is considered by Doxiades and Portius,[6] Davenport [7] and many others to be so small as to indicate strongly that heredity plays no role in the production of the condition.

Doxiades and Portius have been able, however, to obtain accurate adequate verified data concerning 1,682 persons related to 61 with mongolism; they found among these persons 5 cases of mongolism, an incidence of 1:337. According to their earlier calculations, which gave the incidence of mongolism in Germany as 1:7,237, these 5 cases represent a distinctly increased incidence of the condition among the persons most closely related to those afflicted. Schulz [8] found a similar increase of incidence, for among 21 imbeciles and idiots that were relatives of a group of persons with mongolism 3 were found to have the condition. Thus mongolism occurred among this group of feebleminded persons with an incidence of 14.35 per cent. This is distinctly higher than the incidence of 9.3 per cent of mongolism among the total population of the feebleminded persons in Germany, which was determined by Doxiades and Portius [6] on the basis of the assumed incidence of 1:7,237 for the total population and the estimated figure of 100,000 for the total population of feebleminded persons in Germany, of whom 46,000 were institutionalized.

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7. Davenport, C. B.: Causes of Retarded and Incomplete Development, Proc. Am. A. Ment. Deficiency **41**:208-214, 1936.

8. Schulz, B.: Zur Genealogie des Mongolismus, Ztschr. f. d. ges. Neurol. u. Psychiat. **134**:268-324, 1931.

GENERAL ENVIRONMENTAL POSTIMPLANTATIONAL AND IMPLANTATIONAL FACTORS

On the other hand, though it has been shown by the numerous observations of Shuttleworth,[9] Jenkins[4] and Penrose[10] and, most recently, by those of Bleyer,[11] that mongolism tends to appear more frequently among the children of older than among those of younger women, and that, as shown by Davenport and Allen[12] and by Rosanoff and Handy,[13] as well as by other authors, mongolism occurs more frequently in the children of later pregnancies than would be expected on the basis of pure chance, it does not necessarily follow that either the age of the mother, as such, nor the place in the order of birth, as such, has a definitely causal relation to mongolism. Although these authors have shown that among the approximately 0.16 per cent of the women in the general population who sometime during their childbearing period will produce a child with mongolism (Jenkins[4]) about 68.1 per cent (Bleyer[11]) will produce one after reaching the age of 30 years, it is also true that even this proportion gives an extraordinarily small number; for the remaining 99.84 per cent of the women in the general population do not produce children with this condition, regardless of the age or of the number of the pregnancy.

The significance of these data is apparent from a study of the number of births in the United States during the year 1934, for there, according to the figures quoted by Bleyer,[11] of 2,095,939 births, 0.16 per cent, or 3,354 (if we use the figure of Jenkins[4] for the incidence of mongolism in the general population) would have mongolism. Since according to Bleyer[11] 68.1 per cent of these, or 2,284, would be born to women 30 years of age or over, and since the total number of births during the year 1934 to women in the United States who were 30 years of age or over has been quoted by Bleyer to be 541,345, the ratio of 2,284 : 541,345, or 0.422 per cent, indicates the degree of effectiveness of the age of the mother as a direct causal agent in the production of mongolism.

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9. Shuttleworth, G.: Mongolian Imbecility, Brit. M. J. **2**:661-665, 1909.

10. Penrose, L. S.: The Relative Effects of Paternal and Maternal Age in Mongolism, J. Genetics **27**:219-224 (May) 1933; The Relative Aetiological Importance of Birth Order and Maternal Age in Mongolism, Proc. Roy. Soc., London, s.B **115**:431-450 (Aug. 1) 1934; A Method of Separating the Relative Aetiological Effects of Birth Order and Maternal Age, with Special Reference to Mongolian Imbecility, Ann. Eugenics **6**:108-127 (Oct.) 1934.

11. Bleyer, A.: Role of Advanced Maternal Age in Causing Mongolism, Am. J. Dis. Child. **55**:79-92 (Jan.) 1938.

12. Davenport, C. B., and Allen, G.: Family Studies on Mongoloid Dwarfs, J. Psycho-Asthenics **29**:266-286 (May) 1925.

13. Rosanoff, A. J., and Handy, L. M.: Etiology of Mongolism, with Special Reference to Its Occurrence in Twins, Am. J. Dis. Child. **48**:764-779 (Oct.) 1934.

Furthermore, as has been noted by Brousseau,[1] Macklin,[2] Rosanoff and Handy [13] and others, there are numerous cases in which from 1 to 7 or more perfectly normal children have been produced after the birth of a child with mongolism. These observations are further confirmed by the conditions that occurred in the fraternities of the persons with mongolism at Letchworth Village. In that institution, among 259 such persons admitted between March 1, 1921, and March 1, 1938, 97, or 37.4 per cent, occurred in fraternities in which 1 or more normal children were produced subsequently to the birth of the child with mongolism. To be sure, 56 of these fraternities contained only 1 subsequently produced normal sib, but 25 contained 2, 8 contained 3, 3 contained 4, 4 contained 5 and 1 contained 7.

Relation of Actual to Expected Frequency of Births of Children with Mongolism in the Last Birth Position on the Basis of Chance Distribution

	Characterization and Description of the Columns						
	Column 1	Column 2	Column 3			Column 4	
	Number of Persons with Mongolism in the Birth Position, Indicated for All Fraternities	Number of Fraternities with Last Birth in the Position, Indicated for All Fraternities	Number of Births of Persons with Mongolism in the Last Position			Number of Births of Persons with Mongolism in the Position, Indicated from the Last	
Birth Position			*a* Actual	*b* Expected on the Basis of Chance	*c* Difference Between Actual and Expected	*a* Actual	*b* Expected on the Basis of Chance
0	..	..	..	..	..	144	50
1	56	17	17	17	0	57	47
2	43	39	27	20	7	29	39
3	33	44	20	15	5	11	30
4	30	29	17	7	10	7	25
5	23	31	13	6	7	7	19
6	18	26	13	4	9	2	14
7	13	16	7	2	5	1	11
8	9	13	5	1.6	3.4	..	8.4
9	13	12	8	1.3	6.7	1	6
10	11	16	8	1.6	6.4	..	3.8
11	3	6	3	0.5	2.5	..	1.9
12	2	3	2	0.3	1.7	..	1.4
13	2	3	2	0.2	1.8	..	0.77
14	1	1	1	0.07	0.93	..	0.58
15	1	2	1	0.13	0.87	..	0.19
16	1	0	..	0.06	..	..	0.19
17	..	0	..	0.06	..	..	0.19
18	..	0	..	0.06	..	..	0.19
19	..	1	..	0.05	..	..	..

Each of these 169 normal children was born, of course, of a woman who was still older than when she produced the abnormal child, and each was born in such an order as to have a birth rank distinctly higher than that of the child with mongolism. In these determinations, abortions, miscarriages, stillbirths, and infants who died young (if the records merely mentioned the early death) were not considered.

In order to correlate a wide variety of data designed to show the relation of production of children with mongolism to order of birth, the data of such of the Letchworth Village material as is concerned with that question are presented in the table. An examination of this

table shows in column 1 that, as Bleyer [11] found with his data and as has been described by Davenport and Allen [12] and by Brousseau,[1] the number of children with mongolism produced is greatest for the first pregnancy and progressively declines as the number of the pregnancy increases. The number of such first pregnancies, however, is somewhat lower than would be expected on the basis of chance. Yet this situation is not inconsistent with the earlier observations of Davenport and Allen,[12] Rosanoff and Handy [13] and others, who found that infants with mongolism occur more frequently in the last birth position than would be expected on the basis of chance, for, as may be seen in column 2 of the table, several of the first pregnancies also are the last. As may be seen in columns 3*a* and 3*b*, all of the remaining fraternities show a markedly higher number of persons with mongolism in the last birth position than would be expected on the basis of chance; the differences between the actual and the expected values are shown in column 3*c*. This condition is also shown in columns 4*a* and 4*b*, where the number of fraternities with the afflicted person in the last birth position is shown to be nearly three times the number expected on the basis of chance. It is interesting, however, that as shown in column 2 the maximum number of cases of mongolism in persons in the last birth position occurs in the families with 2 children and that the number of such cases progressively decreases as the number of the preceding births increases.

This frequent occurrence of persons with mongolism in the last birth position appears to be rather significant. Certainly it is not directly and entirely due to the advancing age of the mother, as such; for in the Letchworth Village data in 55 of the 144 cases in which children with mongolism resulted from the last pregnancy, the mothers were 35 years of age or younger, while of the 115 cases in which pregnancies followed the birth of an afflicted child, in 34 the women were 35 years of age or older. Certainly, therefore, some of the women whose last child had mongolism would ordinarily be capable of producing more offspring, and the occurrence of pregnancies following the birth of an abnormal child in approximately 44.4 per cent of the cases shows that the condition is not produced by the development of some sort of sterilizing influence in the maternal organism. These conditions suggest that the cause of this sudden cessation in the production of offspring may be highly artificial; perhaps it is a voluntary determination on the part of the parents not to incur the risk, slight as it is, of producing another child with mongolism.

In order to obtain some direct evidence concerning the extent to which weakening of the mother due to successive child bearing might be effective in the production of mongolism, all available data concerning the prenatal physical and health conditions of the mothers of the 259 persons with mongolism were collected. Data concerning 171

mothers were available. In 133 of the cases the prenatal conditions were described as normal, uneventful or favorable and the condition of the mother during the gestational period as healthy, perfectly well, good or excellent. In 9 cases, the mother had medical supervision throughout the period. On the other hand, in only 38 cases was it mentioned that the mother during the gestational period was in poor health, overworked, weakened, tired, miserable, run down or nervous. In 6 cases it was mentioned that the mother was going through the menopause. In but 1 case was there "displacement of internal organs and womb trouble." For these reasons, it is impossible to attribute the mongolism directly to aging of the mother or to exhaustion of the uterus through use, although it is equally true that the condition or conditions that do produce mongolism, whatever they may be, have been shown by Bleyer [11] and others to be more effectively operative, or to occur more frequently, in the older women and therefore to a certain extent in the later pregnancies.

Though it is apparent that permanent, unidirectional, irrecoverable changes in the maternal organism do not have a direct causal effect in the production of mongolism, it is nevertheless possible that temporary, recoverable changes may be more effective. Such changes must take the form of nutritional, endocrine or other disturbances of a qualitative nature in the composition of the blood stream of the mother, for the maternal circulatory system serves as the only medium for gaseous, nutritional and other exchange between the mother and the developing embryo. Since, however, both embryos of a twin pregnancy are provided with nutriment from the same blood stream, it is obvious that disturbances in the composition of such a medium could not selectively affect a single member of the pair.

In the literature, according to Rosanoff and Handy,[13] there are records of 64 cases of mongolism occurring in twins. In 52 of these, the condition appeared in a single member of the pair. In 5 cases neither the sex nor the type could be determined, while of the remaining 47 pairs, 23 were of unlike and 24 were of like sex. In all of the 12 cases in which mongolism appeared in both members of the twin pair, the 2 numbers were of the same sex. According to the difference method of Weinberg,[14] these could be considered as monozygotic, or identical, twins, and 8 of them have been positively identified as such. Doxiades and Portius [6] described 5 additional cases of mongolism in twins. In all of these cases only 1 member was affected. In 4 instances the twins were definitely identified as dizygotic, in 2 by the birth membranes and in 2 by the similarities-dissimilarities method. In 1 case the sex

14. Weinberg, W.: Beiträge zur Physiologie und Pathologie der Mehrlingsgeburten beim Menschen, Arch. f. d. ges. Physiol. **88**:346-430, 1901.

and type were unknown, for the normal member died at the age of 9 months. To these may be added 1 case among the patients at Letchworth Village. These twins were of like sex (female), and only 1 member was affected, but it was impossible further to identify the type from the data available.

It is clear, therefore, that 58 cases of mongolism in twins are positively known to have occurred in which only 1 member was affected. Of the remaining 12 known cases of mongolism in twins, both members were affected. Of these twins, 8 pairs have been definitely identified as identical, and the ratios obtained by the difference method indicate strongly that the remaining 4 pairs also are identical. On the basis of this evidence, it is apparent that temporary, recoverable, nutritional, endocrine or other disturbances of a qualitative nature in the composition of the maternal blood stream cannot bear a directly causal relation to mongolism, and this conclusion is abundantly confirmed by the observations of Davenport and Allen,[12] Brousseau [1] and many others, which show that severe prenatal, emotional, physiologic or physical disturbances of the mother have no definite relation to production of this abnormality. Similar conclusions have been obtained from the data concerning the Letchworth Village cases.

Any differences which might occur in the quantity of nutrient, endocrine or other substances that might be received by the embryo from the mother must depend on the location and the nature of the placentation rather than on temporary variations in the content of the maternal blood stream. Since the nature and location of the placentation are determined at the time of the implantation of the blastocyst, any factors which might operate to produce mongolism in this way would have to act at the time of, or proceed from the nature or location of, the implantation. Nutritional blighting could be expected to result from the operation of such factors. The extent to which mongolism might be attributed to nutritional blighting of the fetus is, to be sure, open to some question. The weights of newborn infants with mongolism, however, are not appreciably lower than those of average normal children, as may be seen from a study of the records concerning the patients with mongolism at Letchworth Village. Of 108 of these, whose weights at birth are available, the average weight was 7.08 pounds (3,211 Gm.). Of these, 18, or 16.65 per cent, weighed 9 pounds (4,082 Gm.) or over. These figures are close to the 7.25 pounds (3,289 Gm.) given by Williams [15] for the weight of the average child at full term. As shown by Davenport and Allen [12] and by the Letchworth Village data, it is clear that practically all those who have mongolism are born at full term. Data concerning the weights of twin pairs 1 member of which is afflicted are somewhat limited. Rosanoff and

15. Williams, J. W.: Obstetrics, New York, D. Appleton and Company, 1925.

Handy,[13] however, give the data for 2 pairs of the twins whom they described. In 1 case the abnormal child weighed 8 pounds (3,629 Gm.) and the normal child 9 pounds; in the other case, "the normal twin weighed a pound less than his mongol brother." These children with mongolism could scarcely be considered to be nutritionally blighted. In the case of another pair of twins described by Rosanoff and Handy, the normal child weighed 16 pounds and 3 ounces (7,343 Gm.), while the abnormal one weighed 17 pounds and 8 ounces (7,938 Gm.) at approximately the age of 9 months. The average normal weight for that age is 18 pounds (8,165 Gm.).

The possible role of the amniotic fluid in the production of mongolism is, of course, unknown. The experiments, however, of Zangemiester (quoted by Williams [15]), Polano,[16] Bondi,[17] Mandl,[18] Goldman [19] and others have shown that the amniotic fluid is derived from a secretory activity of the amniotic epithelium rather than from a direct transudation from the maternal blood. This indicates that there is no direct relation between the amniotic fluid and the maternal blood stream and that changes in the latter would not be expected directly to produce changes in the former. Any effects, therefore, that the composition of the amniotic fluid might have on the developing embryo would not be directly caused by the quantity or by the qualitative composition of the maternal blood stream.

It has been suggested by Jansen,[20] however, that amniotic pressures are the cause of mongolism. He apparently referred not to generalized uterine pressures imposed by the uterine and by the abdominal walls, which could scarcely be expected to exert confining influences selectively on but 1 of the 2 amnions of dizygotic twin fetuses, but rather to distinctly intra-amniotic pressures exerted on the embryo directly by the amniotic walls and by the enclosed amniotic fluid. Jansen (p. 50) stated: "The pressure in the amniotic liquid is enhanced. The blood is squeezed out of the foetus and through the umbilical vessels to the placenta, whence it can enter into the province of enhanced pressure in the amniotic sac only with difficulty. The whole embryo suffers from hunger." Since the amount and pressure of the amniotic fluid

16. Polano, O.: Ueber die sekretorischen Tätigkeiten des amniotischen Epithels, Zentralbl. f. Gynäk. **40**:1203-1206 (Oct. 7) 1905.

17. Bondi, J.: Zur Histologie des Amnionepithels, Zentralbl. f. Gynäk. **29**: 1073-1076 (Sept. 2) 1905.

18 Mandl, L.: Weitere Beiträge zur Kenntnis der sekretorischen Tätigkeit des Amnionepithels, Ztschr. f. Geburtsh. u. Gynäk. **58**:249-257, 1906.

19. Goldman, E. E.: Die äussere und innere Sekretion im Lichte der "vitalen Färbung," Beitr. z. klin. Chir. **78**:1-108 (March) 1912.

20. Jansen, M.: Feebleness of Growth and Congenital Dwarfism, London, Henry Frowde, Hodder & Stoughton, 1921.

have been shown to be directly related to the secretory activities of the amniotic epithelium, where the fluid is originally produced, it is clear that any conditions caused by intra-amniotic pressures, as Jansen believes to be the case with pregnancies resulting in mongolism, definitely must arise in some way from within the implanted ovum.

The complete absence of mongolism in one of the members of all of the known and positively identified pairs of dizygotic twins and the ocurrence of mongolism in both members of all of the known and positively identified pairs of monozygotic twins indicates, as Rosanoff and Handy [13] noted, that the factors which produce mongolism must operate at some stage in the early embryonic development prior to that at which in cases of monozygotic twinning the division into 2 takes place. This division may occur at various stages in the development of the zygote, but the latest stage at which it can occur is that of gastrulation. In man, according to information provided by the embryos of von Möllendorff,[21] Streeter,[22] Spee,[23] Peters [24] and Miller,[25] gastrulation may be considered to occur from eleven to nineteen days after implantation.

It is possible that there are differences in the different portions of the uterine walls and that these cause variations in the serum which accompanies the edematous condition of the decidua, in the products of the digestive action of the trophoblast and in the secretions of glycogen, as shown by Driessen,[26] Wegelin,[27] Ascheim [28] and others, as well as in other substances formed from the uterine glands, all of which serve for the early nutriment of the embryo. Owing, however, to the close relation between the development of the uterine decidua and the production of hormones by the corpus luteum, which has been shown by

21. von Möllendorff, W.: Ueber das jüngste bisher bekannte menschliche Abortivei, Ztschr. f. Anat. u. Entwcklngsgesch. **62**:352-405 (July) 1921; Ueber einen jungen operativ gewonnen menschlichen Keim, ibid. **62**:406-432 (July) 1921.

22. Streeter, G. L.: A Human Embryo (Mateer) of the Presomite Period, Contrib. Embryol. (no. 272) **9**:389-424, 1920.

23. Spee, F. G.: Neue Beobachtungen über sehr frühe Entwickelungsstufen des menschlichen Eies, Arch. f. Anat. u. Entwcklngsgesch., 1896, pp. 1-30; Demontration eines jungen Stadiums der menschlichen Eieinbettung, Verhandl. d. deutsch. Gesellsch. f. Gynäk. **11**:421-422, 1906.

24. Peters, H.: Ueber die Einbettung des menschlichen Eies, Leipzig, Franz Deuticke, 1899.

25. Miller, J. W.: Das jüngste operativ erhaltene menschliche Ei, Berl. klin. Wchnschr. **50**:865-869, 1913.

26. Driessen, L. F.: Ueber Glykogen in der Placenta, Arch. f. Gynäk. **82**:278-301, 1907; Glykogenproduction, eine physiologische Funktion der Uterusdrüsen, Zentralbl. f. Gynäk. **35**:1308-1313 (Sept. 16) 1911.

27. Wegelin, C.: Der Glykogengehalt der menschlichen Uterusschleimhaut, Centralbl. f. allg. Path. u. path. Anat. **22**:1-8, 1911.

28. Ascheim, D.: Ueber den Glykogengehalt der Uterusschleimhaut, Zentralbl. f. Gynäk. **39**:65-70 (Jan. 30) 1915.

Hitschmann and Adler,[29] Schroeder,[30] Williams,[15] Evans,[31] Fraenkel,[32] Halban and Kohler,[33] Meyer,[34] Ruge [35] and others, it is unlikely that any marked local variations occur in the histologic-physiologic structure of an organ that is so highly vascular and so histologically homogeneous as the uterus. Furthermore, as shown by Vincent,[36] Williams,[15] Schmorl,[37] Kinoshita,[38] Hormann [39] and others, the formation of decidual tissue may be widespread and may often include the fallopian tubes, the ovarian mesenteries, the peritoneum and other structures. The decidual tissue is not, therefore, a highly specific structure but instead may develop from the generalized tissues of many organs under proper hormonal stimulation. Furthermore, the studies of tubal and of other extrauterine pregnancies indicate, as shown by Sutton,[40] Futh,[41] Mahfouz [42] and others, that the decidua plays a readily dispensable role in the implantation of such ova. Instead, according to Williams,[15] it is probable that the uterine decidua develops primarily for the protection

29. Hitschmann, F., and Adler, L.: Der Bau der Uterusschleimhaut, Monatschr. f. Geburtsh. u. Gynäk. **27**:1-81, 1908.

30. Schroeder, R.: Ueber die zeitlichen Beziehungen der Ovulation und Menstruation, Arch. f. Gynäk. **101**:1-35, 1914.

31. Evans, H. M.: The Rhythm of Gonadal Function with Special Reference to the Relations Between Uterus and Ovary, in Barker, L. F.: Endocrinology and Metabolism, New York, D. Appleton and Company, 1922, vol. 2, pp. 573-599.

32. Fraenkel, L.: Die Function des Corpus luteum, Arch. f. Gynäk. **68**:438-545, 1903; Neue Experimente zur Function des Corpus luteum, ibid. **91**:705-761, 1910.

33. Halban, J., and Kohler, R.: Die Beziehungen zwischen Corpus luteum und Menstruation, Arch. f. Gynäk. **103**:575-589, 1914.

34. Meyer, R.: Ueber die Beziehung der Eizelle und des befruchteten Eies zum Follikelapparat, Arch. f. Gynäk. **100**:1-19, 1913.

35. Ruge, C.: Ueber Ovulation, Corpus luteum und Menstruation, Arch. f. Gynäk. **100**:20-48, 1913.

36. Vincent, S.: Physiology, Physiological Chemistry, and Experimental Pathology of the Female Gonads (Exclusive of the Mammae and Placenta), in Barker, L. F.: Endocrinology and Metabolism, New York, D. Appleton and Company, 1922, vol. 2, pp. 550-571.

37. Schmorl: Ueber grosszellige (decidua-ähnliche) Wucherungen auf dem Peritoneum und den Ovarien bei intrauteriner Schwangerschaft, Monatschr. f. Geburtsh. u. Gynäk. **5**:46-50, 1897.

38. Kinoshita, S.: Ueber grosszellige decidua-ähnliche Wucherungen auf dem Peritoneum, Monatschr. f. Geburtsh. u. Gynäk. **8**:500-509, 1898.

39. Hormann, K.: Beitrag zur Kenntnis der decidualen Bildungen in den Ovarien, Arch. f. Gynäk. **80**:297-305, 1906.

40. Sutton, J. B.: The Purvis Oration on Abdominal Pregnancy in Women, Cats, Dogs, and Rabbits, Lancet **2**:1625-1627 (Dec. 10) 1904.

41. Futh, H.: Ueber die Einbettung des Eies in der Tube, Arch. f. Gynäk. **63**:97-158, 1901.

42. Mahfouz, N. P.: Ectopic Pregnancy, J. Obst. & Gynaec. Brit. Emp. **45**: 209-232 (April) 1938.

of the maternal tissues from the invasive and corrosive action of the fetal cells, which in normal pregnancies are entirely surrounded by the decidual cells.

These decidual cells, as shown by Williams, Evans and others, are freshly developed immediately before each pregnancy and are directly under the control of hormones from the corpus luteum which circulate in the blood. Since it is therefore probable that all of the decidual tissues are essentially alike and neither highly specific nor indispensably concerned with the development of the embryo, and since no cases are known of the occurrence of mongolism in both members of a pair of fraternal twins, it is unlikely that mongolism could be produced by disturbances in the hormonal mechanism concerned with the formation of the decidua. Hence, it is probable that the factors which lead to the production of mongolism do not operate in the implantational or in the postimplantational-pregastrulational period of the development of the embryo. Davenport [7] concluded that "any theory of a maternal influence acting through the placenta seems to be ruled out."

MATURATIONAL AND TUBAL FACTORS

As in several cases that have already been considered, evidence concerning the determination of the extent to which maturational and tubal factors might operate to produce mongolism is provided, in lieu of direct experimental evidence, from observations concerning the occurrence of mongolism in dizygotic twins. This evidence is distinctly limited, but the conditions that are indicated, if confirmed by more cases, would definitely provide a significant contribution to knowledge concerning the occurrence of mongolism; for it is probable that at least two of the three possible modes of origin of the 2 ova involved in dizygotic twinning, as described by Greulich,[43] are represented among the 58 known cases of such twinning.

In those cases of twinning produced from ova each of which, as shown by Allen and his associates [44] and by others, is supplied from a different ovary, the invariant occurrence of mongolism in but 1 member of the pair indicates that generalized endocrine, nutritional, emotional or other disturbances of the maternal organism which might render abnormal all of the ova produced during a single menstrual cycle could not be directly operative in the production of mongolism. The conclusion is further corroborated by the fact that the mechanism involved

43. Greulich, W. W.: Birth of Six Pairs of Fraternal Twins to the Same Parents, J. A. M. A. **110**:559-563 (Feb. 19) 1938.

44. Allen, E.; Pratt, J. P.; Newell, Q. N., and Bland, L. J.: Recovery of Human Ova from the Uterine Tubes: Time of Ovulation in the Menstrual Cycle, J. A. M. A. **91**:1018-1020 (Oct. 6) 1928.

in the initiation of the development of the graafian follicle and in ultimate ovulation is, as shown by Riddle and Bates,[45] Bates and his co-workers,[46] Schooley and Riddle[47] and others in the case of the pigeon and by several other workers with other animals, clearly under the control of the endocrine factors from the pituitary gland. On the other hand, in cases of twinning produced from ova which, as shown by Greulich,[43] are supplied by the rupture of 2 follicles in 1 ovary, the similar invariant occurrence of mongolism in but 1 member of the pair indicates that intratubal conditions that must operate at some stage in the intratubal life of the ovum or zygote could not of themselves be effective in the production of mongolism.

Other intraovarian conditions which might influence the development and maturation of the ovum in such a way as to lead to the production of mongolism might involve either a gradual and progressive deterioration of the whole ovary, as suggested by Mackintosh,[48] or a specific unique action on a single follicle brought about, as Rosanoff and Handy[13] suggested, by proximity to old sites of corpora lutea or by other means. Evidence concerning these suggestions is provided by the cases of fraternal twinning which might arise from ova produced from within a single follicle, as described by Greulich,[49] Arnold[50] and several others. The similarly invariant occurrence of mongolism in but 1 member of such pairs of twins indicates, however, that intrafollicular conditions which must operate at some time during the development of such ova could not be effective in the production of mongolism. This conclusion is rendered distinctly tentative, however, by the fact that its value is entirely dependent on the proportion of the cases of mongolism in dizygotic twins that would arise from ova produced in that way. This proportion would probably be comparatively small, but the number of twins that would arise from ova produced in each of these three ways cannot be determined from the data available.

It appears, however, from the known facts concerning the formation, degeneration and ultimate absorption and replacement of the corpus

45. Riddle, O., and Bates, R. W.: Concerning Anterior Pituitary Hormones, Endocrinology **17**:689-698 (Nov.-Dec.) 1933.

46. Bates, R. W.; Lahr, E. L., and Riddle, O.: The Gross Action of Prolactin and Follicle-Stimulating Hormone on the Mature Ovary and Sex Accessories of the Fowl, Am. J. Physiol. **111**:361-368 (March) 1935.

47. Schooley, J. P., and Riddle, O.: The Morphological Basis of Pituitary Function in Pigeons, Am. J. Anat. **62**:313-350 (April) 1938.

48. Mackintosh, J. M.: The Etiology of Mongolism, Brit. M. J. **2**:129 (July 21) 1928.

49. Greulich, W. W.: Heredity in Human Twinning, Am. J. Phys. Anthropol. **19**:391-431 (Oct.-Dec.) 1934.

50. Arnold, L.: Adult Human Ovaries with Follicles Containing Several Oocytes, Anat. Rec. **6**:413-422, 1912.

luteum by connective tissue at the site of each ovulation, described by Williams [15] and many others, that the formation of scar tissue in the spaces left by the ruptured follicles is avoided, as stated by Clark [51] and others. The suggestion of Rosanoff and Handy,[13] therefore, that "circumstantial evidence . . . justifies the speculation that foci of tissue change—perhaps scars—marking the sites of old ovulation are the cause of the trouble" is untenable. In older women, however, corpora fibrosa form, which may persist for some time before complete absorption; but these apparently are not what Rosanoff and Handy had in mind.

INTRAGAMETIC NONHEREDITARY FACTORS

So far as the number of cases of twinning is sufficient to justify conclusions, it is definitely demonstrated that the causes of mongolism must reside in some factor or factors that cannot, at any stage of development, act directly on more than 1 ovum or zygote. Such factors must operate, therefore, from within the gametes, and so must be either chromosomal or cytoplasmic. The possible influences that chromosomal factors may have in the production of mongolism have already been considered.

Intragametic, nonhereditary factors that might be influential in the production of mongolism are those which concern the physiologic condition of the cytoplasm and membranes of the egg at the time of fertilization. There is but little information concerning the physiology of fertilization in man. It is known, however, as shown by Thomson,[52] Dixon,[53] Allen and others,[54] Hoadley and Simons,[55] Simkins [56] and Aykroyd,[57] that the ovum is extruded from the ovary during the metaphase of the second maturation division and must be fertilized before maturation can be completed. Fertilization, according to Williams,[15]

51. Clark, J. G.: The Origin, Growth, and Fate of the Corpus Luteum, Johns Hopkins Hosp. Rep. **7**:181-220, 1898.

52. Thomson, A.: The Maturation of the Human Ovum, J. Anat. **53**:172-208 (April) 1919.

53. Dixon, A. F.: Human Oöcyte Showing First Polar Body and Metaphase Stage in the Formation of Second Polar Body, Irish J. M. Sc., April 1927, pp. 149-151.

54. Allen, E.; Pratt, J. P.; Newell, Q. U., and Bland, L. J.: Human Tubal Ova: Related Early Corpora Lutea and Uterine Tubes, Contrib. Embryol. (no. 414) **22**:45-76, 1930.

55. Hoadley, L., and Simons, D.: Maturation Phases in Human Oöcytes, Am. J. Anat. **41**:497-509 (July) 1928.

56. Simkins, C. S.: Textbook of Human Embryology, Philadelphia, F. A. Davis Company, 1931.

57. Aykroyd, O. E.: Cytoplasmic Inclusions in the Oogenesis of Man, Ztschr. f. Zellforsch. **27**:691-710 (March) 1938.

usually takes place in the lateral portion of the tube but occasionally occurs on the surface of the ovary or even in the follicle, as demonstrated by the occurrence of ovarian pregnancies. The length of time that gametes may retain the capacity to be activated or the capacity to activate the egg has not been precisely determined. Although Nürnberger [58] and others have demonstrated that spermatozoa retain their motility in the fallopian tubes for several days, judging from the work of Lillie [59] it is doubtful that they retain their fertilizing power for as long a time.

The length of time that the gametes retain their capacity to activate or to be activated can be determined only approximately and indirectly from the available data. The time of ovulation has been determined by histologic correlational studies of the graafian follicle, corpus luteum and uterine endometrium by Evans,[31] Halban and Kohler,[33] Meyer,[34] Ruge,[35] Schroeder,[30] Simkins [56] and several others, by the vaginal smear method by Papanicolaou [60] and by records of the time of recovery of eggs from the tubes by Allen and his associates [44] and others. From these observations it has been found that ovulation usually occurs in the later days of the second week after the beginning of the preceding period; according to Simkins,[56] who obtained a curve from the data of Asdell,[61] Dickinson [62] and others, fruitful unions may occur at any time up to within one week of the beginning of the next menstrual period. From this it may be calculated that sperm may retain their fertilizing power for as much as seven days in the female genital tracts and that the ovum may retain its capacity to be activated for approximately nine days $(28-[12+7]=9)$. The reliability of these figures, however, depends on the degree of variation that may occur in the time of ovulation, concerning which no definite data are available. It is probable, however, that both spermatozoa and ova retain their capacity to activate or to be activated for an appreciable length of time while in the fallopian tubes and that this capacity is lost gradually but progressively with the passage of time. Samuels,[63] on the basis of cycloscopic observations,

58. Nürnberger, L.: Klinische und experimentelle Untersuchungen über die Lebensdauer der menschlichen Spermatozoen, Monatschr. f. Geburtsh. u. Gynäk. **53**:87-101, 1920.

59. Lillie, F. R.: Problems of Fertilization, Chicago, University of Chicago Press, 1919.

60. Papanicolaou, G. N.: The Sexual Cycle in the Human Female as Revealed by Vaginal Smears, Am. J. Anat. (supp.) **52**:519-616 (May) 1933.

61. Asdell, S. A.: Time of Conception and of Ovulation in Relation to the Menstrual Cycle, J. A. M. A. **89**:509-511 (Aug. 13) 1927.

62. Dickinson, R. L.: The "Safe Period" as a Birth Control Measure, Am. J. Obst. & Gynec. **14**:718-730 (Dec.) 1927.

63. Samuels, J.: The Cycle of the Woman, J. Obst. & Gynaec. Brit. Emp. **45**:291-319 (April) 1938.

stated that the human ovum is capable of fertilization for but two days at most and that 2 ova are frequently produced during each menstrual cycle.

Nothing is known concerning the mechanism of fertilization in man; but so far as the observations of Lillie,[59] Just [64] and several others on the eggs of the sea urchin, nereid worms and numerous other forms of life have value when applied to man, the capacity of an egg for fertilization depends on the presence in the egg cortex of a substance termed fertilizin by Lillie,[59] which, however, is gradually lost, probably by simple diffusion, into the surrounding fluids when the egg is liberated from the ovary. As shown by Lillie and others, when all of this substance has been rapidly removed by repeated washing, the eggs can no longer be activated, even though they appear to be perfectly healthy and normal in every other way. Thus the ovum, beginning at the time of its extrusion from the ovary, undergoes a progressive process of deletion of this substance. This process can be terminated only by some sort of activation; otherwise it follows a definite course until finally the completely inactivable state is reached. Goldforb [65] has found that the amount of egg substances produced first increases and then rapidly decreases.

That the fertilizing power of the spermatozoa depends similarly on a substance borne on the sperm head, possibly the acrosome, as suggested by the work of Bowen,[66] Parat [67] and Wintrebert,[68] is shown by the numerous observations described by Lillie [59] concerning the effect of dilution on the fertilizing power of the sperm. These observations were confirmed and extended by the experiments of Barthelemy,[69]

64. Just, E. E.: Fertilization Reaction in Echinarachnius Parma, Biol. Bull. **36**:1-38 (Jan.) 1919.

65. Goldforb, A. J.: Variation of Normal Germ Cells: Studies in Agglutination, Biol. Bull. **57**:333-349 (Dec.) 1929; Changes in Agglutination of Ageing Germ Cells, ibid. **57**:350-388 (Dec.) 1929; Factors That Change Agglutinability of Ageing Sperm, ibid. **57**:389-411 (Dec.) 1929.

66. Bowen, R. H.: On the Acrosome of the Animal Sperm, Anat. Rec. **28**: 1-13, 1924.

67. Parat, M.: A propos de l'organization du spermatozoïde, Compt. rend. Soc. de biol. **113**:313-314 (May 20) 1933; Nomenclature, genese, structure et function de quelques elements cytoplasmiques des cellules sexuelles males, ibid. **112**:1131-1134 (March 25) 1933; L'acrosome du spermatozoïde dans la fecondation et la parthenogenese experimentale, ibid. **112**:1134-1137 (March 25) 1933.

68. Wintrebert, P.: La fonction enzymatique de l'acrosome spermien du Discoglosse, Compt. rend. Soc. de biol. **112**:1636-1640 (April 29) 1933; Phénomènes d'attraction réciproque des gamètes, de captation et de réception du spermatozoïde par l'ovule, chez Discoglossus pictus Otth., ibid. **105**:520-524 (Nov.) 22) 1930.

69. Barthelemy, H.: Influence de la dilution du sperme sur la duree de survie des spermatozoïdes de la grenouille rousse, Compt. rend. Acad. d. sc. **177**:1068-1070, 1926.

Drzewina and Bohn,[70] Gray,[71] Southwick [72] and others, in which the substance was presumably removed rapidly from the sperm heads by dilution, by certain toxic substances or, in the work of the last-mentioned author, by the egg secretions. The nature of the loss of fertilizing power produced by the effects of dilution and by treatment with egg–sea water was indicated by the experiments at Bermuda with Toxopneustes and Echinometra. Goldforb [65] found that the amount of this spermatic substance produced first increases and then decreases.

The manner in which this substance is lost from either the egg or the spermatozoon is quite unknown, except for the work of Goldforb, as is also the situation concerning the minimal amounts of these substances that are essential for complete activation. However, the results of activation when the amounts of these substances are, presumably, somewhat less than those required for complete activation are indicated by the work of Dungay [73] and Gemmil.[74] Dungay stated:

> It seems that injury, by heating to 44 C., or by ageing, produces a general decrease in vitality, which may manifest itself by a retarded development, by a high mortality, or by the production of forms which are more or less abnormal in structure or behavior. In *Nereis,* at a period of elongation following the trochophore stage, there is a production of abnormalities in the posterior region . . . twenty-five per cent were in various stages from the trochophore to the formation of the second set of larval setae. Some seemed normal in every way except that their development was retarded. Others were less active. Perhaps 5 per cent seemed as far along as the controls, but had no setae or were deficient in some other way.

Of Arbacia he stated: "Many abnormal gastrulae appear." Gemmil [74] found that activation of aged gametes of Nereis or Arbacia often leads to the production of various sorts of abnormalities.

If one assumes that in man, as in other forms of life, fertilization is effected by means of a union of substances borne by the spermatozoon with substances borne by the egg and that these substances are lost

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70. Drzewina, A., and Bohn, G.: Effets tardifs de la dilution du sperme sur le developpement de l'oeuf d'Oursin, Compt. rend. Acad. d. sc. **177**:79-81, 1923; Variations dans le temps du pouvoir fecondant du sperme d'Oursin traité par des substances nocives, en rapport avec son degree de dilution, Compt. rend. Soc. de biol. **89**:383-386, 1923.

71. Gray, J.: The Effect of Dilution on the Activity of Spermatozoa, Brit. J. Exper. Biol. **5**:337-344 (June) 1928; The Effect of Egg Secretions on the Activity of Spermatozoa, ibid. **5**:362-365 (June) 1928.

72. Southwick, W. E.: The Effect of Egg-Sea-Water on the Physiology of the Spermatozoa of Arbacia Punctulata, Thesis, Harvard University, 1933; Physiology of Spermatozoa, in Annual Report from the Bermuda Biological Station for Research, Inc., 1933.

73. Dungay, N. S.: Effects of Injury upon Sperm, Biol. Bull. **25**:213-260, 1913.

74. Gemmil, J. F.: On the Vitality of the Ova and Spermatozoa of Certain Animals, J. Anat. & Physiol. **34**:163-181 (Jan.) 1900.

gradually by diffusion into the tubal fluids as soon as the gamete leaves the gonad or seminal vesicle, and if one assumes further that, as has been shown to occur in Nereis and Arbacia, an incompletely activated egg, produced by an insufficient quantity of such substances in the gametes at the time of fertilization, causes the appearance of certain rather definite abnormalities in the resulting embryo, it is by no means inconceivable, in view of the evidence already presented, that some of these abnormalities might comprise the condition resulting in mongolism. Unfortunately, there is but little information concerning the mechanism of fertilization, even in nonhuman forms of life, and so far as is known no experiments have been performed to determine the nature, behavior or occurrence of the spermatic substance, other than those which have demonstrated its presence. However, again it is by no means inconceivable that the initial quantity or the rate of loss of the spermatic substance might be differentially determined or affected in the spermatozoon in accordance with the reciprocal presence or absence of the x chromosome or of the y chromosome. Faust [75] described the occurrence of the dimorphism in size of adult spermatozoa of Anasa tristis, while Parkes,[76] basing his conclusion on a count of 235 spermatozoa, observed similar dimorphism in man. Moench and Holt [77] gave a detailed description of some microdissectional studies of human spermatozoa, but they observed no dimorphism in size.

Certain it is, however, as shown by Ciocco,[78] that the still unexplained deviation of the sex ratio in man from the expected value of 100:100 persists in an increasingly accentuated form when premature births, stillbirths, miscarriages and abortions are considered. This might indicate that a larger proportion of incomplete activations are produced by the spermatozoa bearing the y chromosomes and that the spermatozoa bearing the x chromosomes tend to produce either complete activation or no activation. Certain it is, too, that the sex ratio among persons with mongolism has been shown, by data summarized by Orel,[79] Doxiades and Portius [6] and numerous other workers, to range between approximately 148:100 (Orel) and 138:100 (Doxiades and Portius).

75. Faust, E. C.: Size Dimorphism in Adult Spermatozoa of Anasa Tristis, Biol. Bull. **25**:287-303, 1913.

76. Parkes, A. S.: Head Length Dimorphism of Mammalian Spermatozoa, Quart. J. Micr. Sc. **67**:617-625 (Dec.) 1923.

77. Moench, G. L., and Holt, H.: Microdissection Studies of Human Spermatozoa, Biol. Bull. **56**:267-273 (April) 1929; Some Observations on Sperm Dimorphism, ibid. **57**:267-271 (Nov.) 1929.

78. Ciocco, A.: Variation in the Sex Ratio at Birth in the United States, Human Biol. **10**:36-64 (Jan.) 1938.

79. Orel, H.: Zur Aetiologie des Mongolismus, Ztschr. f. Kinderh. **42**:440-452, 1926.

Rosanoff and Handy [13] demonstrated that the contrast is even more marked between twins of opposite sex for among the 23 cases of such twins reported in the literature the boy was affected in 14 instances and the girl in 9. This gives a sex ratio of 156 : 100. Among the 259 cases at Letchworth Village a ratio of 137 : 100 was obtained. In one year, however, among these cases, of 19 patients admitted, 18 were female.

On the basis of these suggestions, it appears that the cause of mongolism could reside in the abnormalities produced by fertilization with gametes, 1 or the other of which might have been in the interphase period which is transitional to the inactivable or nonfunctional state. Whether both gametes or only 1 could thus be effective in producing mongolism has not been determined. The sex ratios, however, as already described, definitely indicate that the spermatozoa might act in such a way, and so far as this statement could be considered to be an accurate identification of the cause of mongolism, it would follow that the rarity of the condition would indicate a short duration for the interphase period. From this it would follow too that such an interphase period might be longer in the case of gametes produced by older parents. Since, however, it has been shown by Penrose,[10] Bleyer,[11] Jenkins [4] and several others that the production of children with mongolism is related to the age of the mother but not to the age of the father, such a lengthening of the interphase period could probably occur only in the case of the ova.

To an extent, too, the applicability of this suggestion is further indicated by the work of Jenkins,[4] who found that when the logarithm of the incidence of mongolism is plotted against the age of the mother a sharp break occurs at about the age of 32 years. The proportion of total births which result in mongolism behaves as a logarithmic function of the age of the mother, beginning with the age of 32 years; below that point the incidence appears to be independent of maternal age. If the length of the interphase period of the ovum should thus be shown to increase as a logarithmic function of the maternal age, as is conceivable, then rather clearcut confirmatory evidence concerning the validity of the suggestion presented in this paper would be obtained.

It would follow from this too that any failure to take all reasonable precautions in order to prevent the simultaneous occurrence of gametes one or the other of which could be expected to be in the interphase stage might tend to increase such opportunities for the production of mongolism.

Direct injuries to the gametes, however, that might be produced by residua from chemical contraceptives that remain in the female genital

tracts, as suggested by Lenz and others,[80] Husler,[81] Stoeltzner[82] and others, has not been confirmed by the observations of Doxiades and Portius,[6] who found when they questioned 61 mothers of persons with mongolism concerning the use of birth control measures that 30 per cent of them used only mechanical methods while but 3, or 5 per cent, used chemical contraceptives before the decision to have a child. Suggestions that some sort of injuries to or abnormalities in the germ cells or in the fertilized egg may cause a tendency toward mongolism have been made by Orel,[79] McLean,[83] Mackintosh,[48] Jenkins[4] and others. It is difficult to discern how such postulated injuries could be produced, except by syphilis, tuberculosis, alcoholism, contraceptional residua or other similar agents, all of which have been shown by Brousseau,[1] Doxiades and Portius[6] and others to have been ineffective in the production of mongolism.

SUMMARY

In the belief that a knowledge of the exact time of the operation of the factor or factors which lead to the production of mongolism would markedly facilitate progress toward an understanding of the etiology of this condition, the various stages of development from the time of the formation of the gametic chromosomes to the time of delivery have been successively considered. Although the available data are not sufficient to allow one to make a definite and final conclusion, it can be stated, on the basis of the conditions found in all of the 58 cases of mongolism in dizygotic twins, that the causes of mongolism must reside in some factor or factors that cannot at any stage of development act directly on more than 1 ovum, zygote or embryo. Since it has been shown that at all stages of development 2 or more ova, zygotes, or embryos may occur in exactly the same external environment, one can conclude that the condition can develop only from within the gametes and so must be either chromosomal or cytoplasmic.

No completely satisfactory determinations of the incidence of mongolism in any general population or in the groups of persons most closely related to an afflicted person have been made. However, the extreme infrequency of cases in which 2 or more persons with the condition appear in one family (in view of the large number of known cases of mongolism, each of which provides an opportunity for such an occur-

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80. Lenz, F., in Baur, E.; Fischer, E., and Lenz, F.: Menschliche Erblehre, ed. 4, Munich, J. F. Lehmanns Verlag, 1936, vol. 1, p. 441.

81. Husler, J., in von Pfaundler, M., and Schlossmann, A.: Handbuch der Kinderheilkunde, ed. 3, Leipzig, F. C. W. Vogel, 1924.

82. Stoeltzner, W.: Der Mongolismus vor und nach dem Weltkriege, Med. Klin. **31**:201-202 (Feb. 15) 1935.

83. McLean, S. J.: Mongolian Idiocy in One of Twins, J. A. M. A. **78**:13-15 (Jan. 7) 1922.

rence) is considered to justify a tentative conclusion that mogolism is not produced by hereditary factors. The factors therefore are not considered to act at the time of the formation of the gametic chromosomes.

The intragametic, nonchromosomal factors that may operate in the production of mongolism appeared to center principally around an aging process that begins at the time of liberation of the gamete from the gonad and terminates at the time of fertilization or with the attainment of a nonfertilizable, nonfunctional condition. It is suggested that, so far as work on Nereis, Arbacia and other forms of life has value when applied to man, this process may be definitely associated with substances liberated from the ovum and from the spermatozoon and that mongolism may be the result of fertilization in which 1 or the other gamete was in an aged condition transitional to the nonfunctional or inactivable state. That the spermatozoa may thus be effective is shown by the abnormal sex ratio that occurs among those with mongolism, and that the ovum may be similarly effective is shown by the definite relation between the age of the mother and the frequency of production of mongolism.

The study was based on the records of 259 persons with mongolism who were admitted to Letchworth Village between 1921 and 1938.

Case Reports

OSTEODYSTROPHIA FIBROSA

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Considerable interest is being taken at present in a syndrome characterized by precocious puberty, pigmentation of the skin and an unusual type of generalized fibrocystic disease of the skeleton. In a recent article McCune and Bruch [1] presented a detailed description of this entity, which they termed osteodystrophia fibrosa. In their résumé of the literature [2] they stated that 14 cases of the condition had been reported to date. The presentation of our 2 cases contributes nothing new to the etiology of the condition, but the cases are of interest as abnormal values for cholesterol, blood fat and blood sugar were found.

REPORT OF CASES

CASE 1.—J. P., a girl, was first admitted to the Hospital for Sick Children on July 4, 1934. At this time she was 10 years of age. The mother of the patient was 34 years of age at the birth of the child and the father 44 years. Both parents were healthy. One brother and two sisters were alive and well. The patient had had no other illness except scarlet fever at the age of 7 years and chickenpox at

From the Department of Paediatrics, University of Toronto, and the Hospital for Sick Children.

1. McCune, D. J., and Bruch, H.: Osteodystrophia Fibrosa: Report of a Case in Which the Condition Was Combined with Precocious Puberty, Pathologic Pigmentation of the Skin and Hyperthyroidism, with a Review of the Literature, Am. J. Dis. Child. **54**:806 (Oct.) 1937.

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6 years. She was born at full term, weighing 7 pounds and 15 ounces (3,600 Gm.), and labor was normal. The child was nursed until the age of 11 months. From that time until the age of 2 years she received cow's milk, cereals, meat, vegetables and fruit. She had 1 fluidrachm (3.7 cc.) of cod liver oil daily from 8 months to 16 months. At the time of admission she was receiving 4 fluidrachms (14.8 cc.) daily. No digestive upsets occurred at any time. She stood alone at 12 months and walked with a normal gait at 16 months. She had her first tooth at 8 months.

There was no history of jaundice at birth, but at or before the age of 12 months a brownish pigmented area was observed on the left arm and left shoulder. At 3 years it was noticed that the child walked with a waddling gait. A diagnosis of coxa vara was made. A roentgenogram taken at this time showed several rarefied areas in the long bones of the legs. The girl started to menstruate every one to three months, the flow lasting four to five days. No menstruation occurred between the ages of 8 and 9 years, but it started again at 9 years. There was some dysmenorrhea with each period. At 5 years there was marked anterior bowing of the left leg, and a lump was felt on the skull over the area of the left occiput. Simultaneously pubic hair was noticed, and the breasts developed. The child's voice became noticeably deeper. Roentgen study of the chest at this time revealed enlargement of the thymus, for which the girl was given roentgen treatment. At the age of 6 years she fractured her right femur. Union took place quickly. At 7 years the child fractured her left humerus, and a swelling was noticed on the right leg below the knee. At 8 years she fractured the left femur; bony union was again rapid. Since the age of 3 years the child had been crying out suddenly for no apparent cause. She was mentally alert, being just one grade behind her age requirement. The retardation might be explained by the loss of considerable time from school. She had always complained of being tired and short of breath after exercise. Myopia was discovered at 8 years. Her hearing had always been good.

The patient (fig. 1) weighed 90 pounds (40.8 Kg.). She was well developed, well nourished and of rather masculine appearance. The mouth was large, and the lips were thick. There was secondary sexual development consisting of pubic hair with normal female distribution and enlargement of the breasts. The skin was not of unusual thickness or coarseness. There was a brownish irregular pigmentation of the skin in the region of the left shoulder; it was not raised above the surface. The hair was not dry or coarse. The head appeared large, and over the occiput several bony prominences and irregularities were felt. The face was broad and asymmetric, the left side being heavier and more prominent than the right. The standing height was 60 inches (152 cm.) and the sitting height 33 inches (84 cm.). The left leg measured 30 inches (76 cm.) and the right 30½ inches (77 cm.). The right leg was longer and better developed than the left, the right thigh being ¼ inch (0.6 cm.) larger than the left. There was an apparent shortening of ½ inch (1.3 cm.), and to compensate for this the pelvis tilted when the girl was standing. There was marked genu valgum. Both tibias were abnormally developed and bowed anteriorly like a saber blade, and both upper extremities showed some bowing. The child had difficulty in walking and used crutches or a wheel chair. The teeth were all present; the upper incisors were equal in size, square and widely spaced. No abdominal masses were palpated. The heart was normal; the systolic blood pressure was 120 mm. of mercury and the diastolic 84 mm.; the pulse rate varied from 90 to 108 beats per minute. On examination the child seemed nervous and apprehensive. Psychometric examination

showed a chronologic age of 10.9 years, a mental age of 11 years and an intelligence quotient of 102. The comment was made that the child was mature in her reasoning. The reflexes were normal and equal throughout. On the left there was suggestive weakness of the flexors of the thigh, the flexors of the lower part of the leg and the extensors of the foot as compared with the muscles on the right. The external genitalia were well developed, the labia minora being hypertrophied.

Roentgenograms of the pelvis and the upper third of each femur were taken in April 1928, when the child was 4 years of age. These showed practically no swelling of the bones and no areas of cystic formation. In both the pelvis and the femurs there were irregular areas of density that lacked all bony markings. In July 1934 the skeleton was completely examined and the report of the skeletal changes was made by Dr. Rolph, the hospital radiologist. The abnormal condition noted in the bones during the patient's previous admission had become much more extensive in its distribution. The necks of the femurs showed no marked change, although a considerable degree of coxa vara had developed. The shafts of the femurs, however, showed much greater density, the whole length of each shaft being involved in marked changes, with a tendency toward cystic formation in many places. The upper half of the right femur had a greatly swollen appearance and some irregular deformity suggestive of a healed fracture. The pelvis had also become greatly deformed, being flattened and twisted badly; the bones comprising it showed a loss of their normal architecture, with fairly uniform density throughout the ilia, but the pubes and ischia showed pseudocystic formation.

A considerable degree of scoliosis had occurred, presumably caused by the deformity and twisting of the pelvis. The tibias and fibulas showed marked change. As in the femurs, the cortex in each of these bones had been greatly thinned out, the shaft had been expanded throughout much of its length, and most of the bone had a curiously pastelike appearance. In many places cystlike changes were observed in both tibias, and in the left fibula marked forward bowing had occurred. No marked changes were shown in the spine. The epiphysial plates were beginning to ossify. The ninth thoracic vertebra showed a distinct diminution of the vertical height of the anterior portion of its body, but no other definite change could be made out in it.

Both humeri showed marked change. The same process appeared to be taking place in them as in the bones of the lower extremities. The cortex of each had been greatly thinned out, and the internal architecture had been destroyed, which gave the bone a pastelike appearance; there was a certain amount of cystic change, particularly in the upper half of each humerus. Slightly below the middle of the left humerus, one curious small compact island was shown. This was larger than the islands usually seen in bones and had a cotton wool appearance, resembling formations frequently seen in Paget's disease. Both radiuses showed changes similar to those of the humeri and femurs, but the ulnas were comparatively unaffected. The long bones of the right hand showed practically no change, but in the left hand all of the bones of the second and the third digit, including their metacarpal bones, showed well marked changes. In the feet, most of the metatarsal bones and most of the proximal phalanges showed similar changes. The cystlike changes in the bones were like those of hyperparathyroidism, but the fibrotic changes characteristic of that condition were replaced by a structureless, pastelike formation which seemed to precede the cystic change.

Examination of the skull revealed marked changes, mostly of a proliferative type, but there were also patchy changes of density throughout the vault of the

skull. The posterior and inferior portions of the cranial walls showed marked thickening, the greatest being in the occipital region; here it reached a maximum a short distance posterior to the foramen magnum, where it formed a marked protuberance fully 1 inch (2.5 cm.) thick. The base of the skull showed increased density and definite thickening except in the frontal region, where practically no proliferation appeared to have taken place. The facial bones showed no definite

TABLE 1.—*Laboratory Findings for J. P.*

Subject of Test	Results of Test		
	July 1934	January 1935	May 1937
Contents of urine	Normal	Normal	Normal
Concentration of urine	Within normal limits	.....	.....
Mantoux reaction	Negative	Negative	.....
Red blood count	.....	5,120,000	5,000,000
Hemoglobin	80%	86%	90%
White blood count	9,600	8,200	11,200
Polymorphonuclears	70%	67%	70%
Lymphocytes	30%	33%	30%
Calcium per 100 cc. serum	9.2-9.6 mg.	12 mg.	10.4 mg.
Phosphorus per 100 cc. serum	3.4-3.5 mg.	3.9 mg.	3.2 mg.
Phosphatase	37-77.7 units	240 units	75.2 units
Cholesterol per 100 cc. whole blood (fasting)	174 mg.	188 mg.	205 mg.
Basal metabolic rate (Benedict and Talbot)	110%	.....	114%
Blood iodine	2.04 per 100 cc.	.....	.....
Nonprotein nitrogen	.....	.....	29 mg. per 100 cc. blood
Creatinine	.....	.....	1.24 mg.
Chlorides	.....	.....	1.01 cc. N/10
Dextrose tolerance			
Blood sugar during fasting	89 mg.	.....	93 mg.
½ hour later	100 mg.	.....	120 mg.
1 hour later	143 mg.	.....	162 mg.
2 hours later	118 mg.	.....	210 mg.
3 hours later	83 mg.	.....	100 mg.
Gonadotropic principle in content of urine	None	.....	.....
Estrogen content of urine	Trace	.....	.....
Cholesterol tolerance (4 Gm. cholesterol in 50 cc. of olive oil)	.....	.....	During fasting, 256 mg.; 8 hours later, 220 mg.; 12 hours later, 224 mg.
Fat tolerance, 8 oz. (30 cc.) 32% cream	.....	.....	During fasting, 247 mg.; ½ hour later, 276 mg.; 1 hour later, 247 mg.; 2 hours later, 330 mg.; 3 hours later, 348 mg.
Calcium balance with intake of 0.1 Gm. calcium per day	.....	.....	There was a negative calcium balance of 0.1515 Gm. daily; urinary excretion of calcium was 10% of total excretion of calcium
Calcium balance with intake of 1 Gm. calcium per day	There was a negative calcium balance of 0.624 Gm. per day; 6% of total calcium was excreted in urine		

change. The outer surface of the thickened portion of the skull appeared to be smooth and of even density. The changes most closely resembled those described as occurring with that form of Paget's disease called osteitis fibrosa localisata.

Pyelography by intravenous injection revealed nothing abnormal in the kidneys or ureters.

The only abnormal laboratory findings (table 1) were an increased basal metabolic rate, an increase in the phosphatase content of the blood and a slightly negative calcium balance.

No diagnosis was made, but it was thought advisable to explore for parathyroid enlargement. No parathyroid tumor was found. When the child was

discharged she was receiving Mead's mineral tablets (alfalfa ash 4 per cent, dicalcium phosphate 32 per cent, and edible bone meal 64 per cent) and 10 minims (0.61 cc.) of viosterol twice a day.

The child was readmitted to the hospital in February 1935, six months later, for further observation. In the interval the parents had noticed little change in her condition, except that she was able to walk without a cane or crutches. The gait was still waddling. The systolic blood pressure was 118 mm. and the diastolic 80 mm. of mercury.

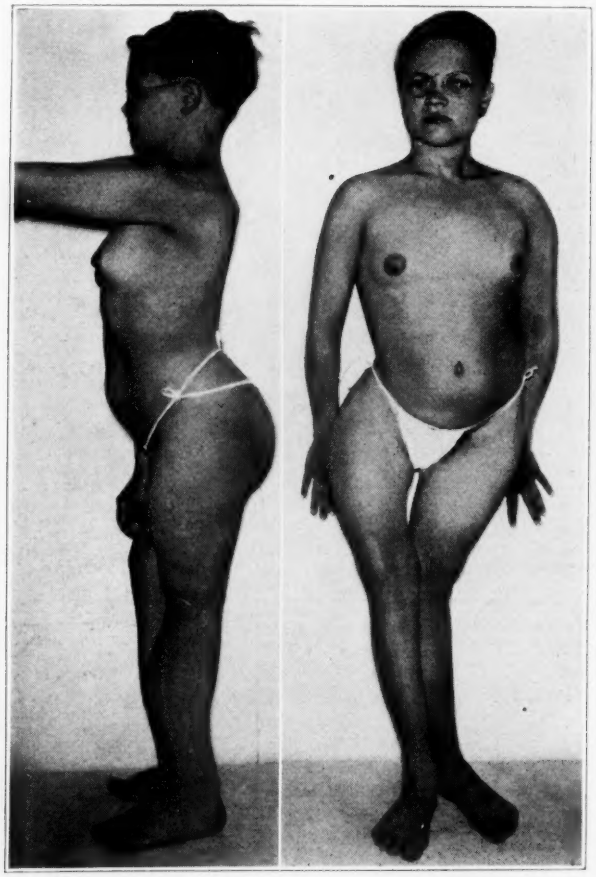

Fig. 1.—J. P., aged 13 years, in May 1937.

Roentgen examination of the skeleton was again done, but little difference from previous roentgenograms was found.

Laboratory tests were done (table 1). It was apparent that during the past five months there had been a slight increase in the calcium, the phosphorus, the cholesterol and the phosphatase content of the blood Physically the child had improved, as she could walk without support.

The girl was admitted to the hospital for the third time in May 1937, two years and nine months after the first admission. She was 13 years of age. There had been no change in her condition since the previous admission. The child had

been menstruating every twenty-one days during the past year. The menstrual period had lasted four or five days, with a scanty flow. During the past year the girl had become more short sighted. Reexamination of the physical condition revealed no striking changes. The patient weighed 102 pounds (46.3 Kg.). A lump was palpated in the left parietal region as well as over the occiput. The pulse rate was 80 to 100 per minute. The psychometric test showed that the chronologic age was 13.7, the mental age 12.8 and the intelligence quotient 94.

On roentgen examination (fig. 2) the softening process appeared to have increased in most of the long bones, and more cystlike formations were seen. The architecture of the heads of some of the bones had been disturbed where formerly no changes were observed. The necks of the femurs had given way further, so that the angle formed by the lower border of the neck with the shaft was only

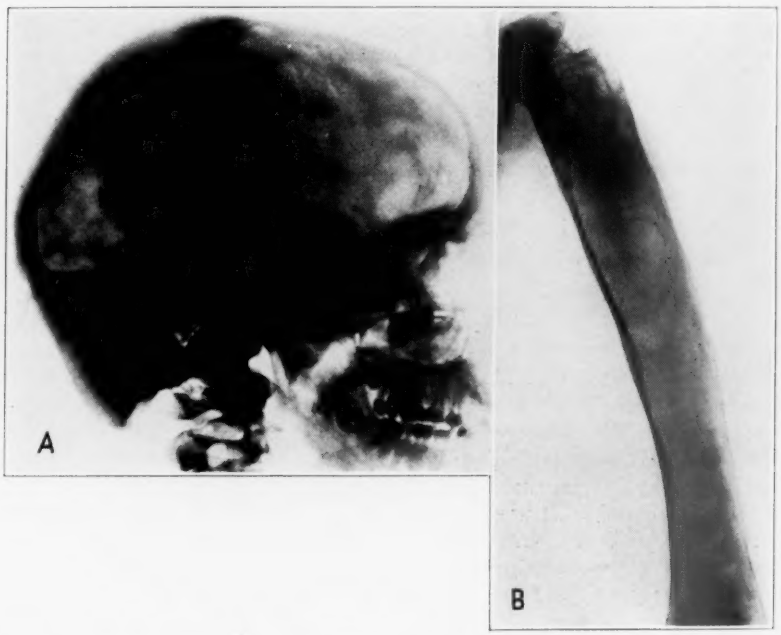

Fig. 2.—Roentgenograms of J. P. *A*, the skull in May 1937. There is considerable thickening, especially in the occipital region; patchy changes of density are seen throughout the vault. *B*, the humerus in July 1937. Progressive changes of marked fibrocystic nature have taken place.

about 45 degrees, and cystlike changes were seen throughout both the shafts and the heads of the bones. The pelvis had collapsed even further: It was twisted and flattened to such an extent that the anterior surface of the sacrum appeared almost to touch the surface of the iliac fossa on the left. There was corresponding scoliosis in the lumbar part of the spine. In the tibias cystlike formations were more marked than before, and the forward bowing had become extreme. Similar changes were shown in the radiuses, but the ulnas still appeared almost normal. Some cystlike areas could now be seen in some of the carpal bones. Cystlike changes were also more marked in the upper half of each radius. Thickening of

the skull had proceeded and now involved the frontal bone and all the floor of the anterior fossa as well as the other parts previously noted.

The laboratory findings showed that changes had occurred during the preceding twenty-one months. This was most noticeable in the sugar tolerance curve, in the increased basal metabolic rate and in the definitely increased cholesterol content of the blood. Because of these high values it was thought that the syndrome was one of xanthomatosis as described by Snapper and Parisel.[2g] In the hope of verifying this diagnosis a biopsy was done by the hospital pathologist, Dr. Erb, on a piece of bone removed from the upper third of the right tibia. It was observed in the gross specimen that the cortex was thinner and softer than usual. The bone marrow was much more solid than ordinary and slightly yellow. Microscopically the periosteum appeared healthy and showed no inflammatory change. The bulk of the section was composed of numerous fine trabeculae of new bone, which had replaced the normal marrow cavity, and cancellous bone. The fine trabeculae were separated by relatively large areas of vascular connective tissue. The cells composing this connective tissue were spindle shaped, and in them no inflammatory cells, giant cells or foam cells could be seen. There was no evidence of cystic change in the bone.

The cholesterol content of the bone was 0.26 per cent and the fatty acid content 0.72 per cent.

During this admission high voltage roentgen therapy was administered. The child was discharged, to return in six months for roentgen examination of the bones.

CASE 2.—J. McK., a girl, was first admitted to the Hospital for Sick Children on March 22, 1937, at the age of 6 years. There was nothing of importance in the family or the personal history. The diet was normal, except that the child ate no raw fruit. There was a history of jaundice at birth which lasted four months. When this had disappeared, a brownish pigmented area was left on the right side of the face, especially around the right eye. At the age of 2 years the child commenced to menstruate. The flow occurred every three to six months and lasted two weeks. It was scanty and was accompanied by crampy pains. The patient first walked at about the age of 2 years, but her gait was always awkward. The right leg was weaker than the left, which resulted in a limp. The child always perspired freely and had cried out in her sleep for the previous four years. Every few months there developed a few pinpoint spots on the arms and legs which were extremely itchy and bled freely. This rash was not associated with the ingestion of any particular food.

The child (fig. 3) weighed 62½ pounds (28.3 Kg.). She was extremely well developed and appeared to be much older than the stated age. There was secondary sexual development, consisting of pubic hair and enlargement of the breasts. There was apparent enlargement of the skull, which measured 20.1 inches (51 cm.) in circumference, and the frontal bones were prominent; the top of the head was almost perfectly flat. The scalp was clear; no exostoses or depressions were felt; the fontanels were closed. There was a brown impalpable discoloration of the skin about the left eye, extending downward to the angle of the mouth and back to the ear on the right side. On the left side, over the zygoma, there was a small patchy area of brown discoloration about the size of a 25 cent piece. There were several similar brown patches over the skin of the back. No petechiae were seen. The eyes, nose and mouth were normal. The thyroid gland was not palpably enlarged; the trachea was in the midline, and no swelling in the neck suggestive of parathyroid tumor was palpable. There

were no enlarged lymphatic glands. The examination of the chest gave normal findings. The heart was not enlarged, and the cardiac sounds were regular and of good quality. There was a soft blowing aortic diastolic murmur propagated down the left side of the sternum. A harsh, not loud aortic systolic murmur was heard along the great vessels. The systolic blood pressure was 140 and the diastolic 75 mm. of mercury. The abdomen was symmetric and moved freely on respiration. There was no tenderness or rigidity. The liver, spleen and kidneys were not palpable, and no masses were felt. The hernial sites were clear. The child was garrulous; her voice was deep. She cried easily. The cranial nerves

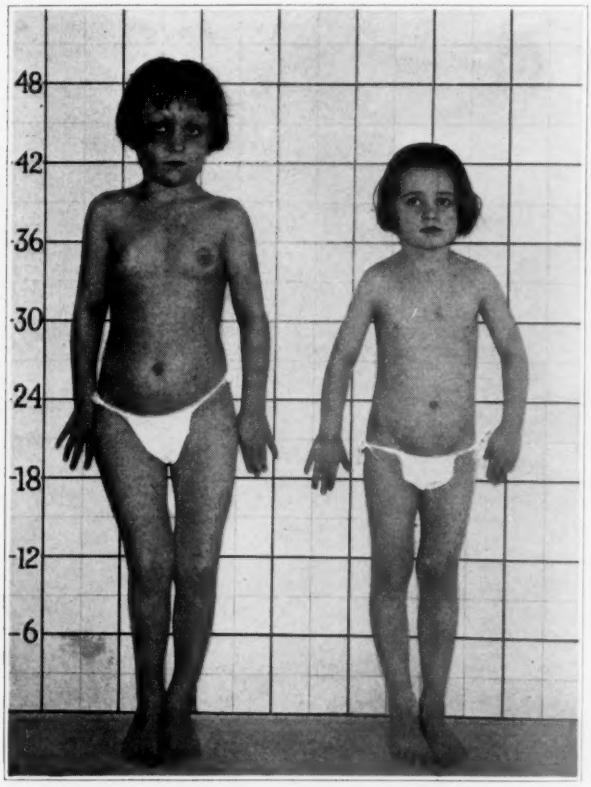

Fig. 3.—J. McK., aged 6 years, in March 1937, with a normal child of the same age.

were normal according to rough tests. The ocular fields could not be tested because the patient would not cooperate. The fundi were not seen, for the same reason. There was no disturbance in sensation to pinprick and light touch. There was no weakness or wasting of the muscles. Coordination and the results of the heel to patella and finger to nose tests were fairly good. Biceps, knee and ankle jerks were present and active bilaterally. Abdominal reflexes were present and active. Psychometric examination showed that the chronologic age was 6.2, the mental age 4.4 and the intelligence quotient 70. There was well marked genu valgum of the right leg. The standing height of the child was 49 inches (124

cm.). The right leg measured 24½ inches (62 cm.) in length, 14½ inches (37 cm.) in circumference at the thigh and 10 inches (25 cm.) in circumference at the calf. The left leg measured 24 inches (61 cm.) in length, 13¾ inches (35 cm.) in circumference at the thigh and 9½ inches (24 cm.) in circumference at the calf.

Roentgen examination (fig. 4) of the entire skeleton was made. Dr. Rolph reported the abnormalities. Marked changes were shown in the bones of the skull. The inner table of the cranial vault stood out as a thin, well defined layer of somewhat irregular form, and on it the rest of the bone was heaped up to a remarkable thickness without differentiation between the diploe and the

Fig. 4.—Roentgenograms of J. McK. taken in March 1937. *A*, the skull shows marked thickening in the parietal and occipital areas. *B*, the humerus shows swelling, loss of trabeculation and areas of thinning.

outer table. This thickening of the calvarium was particularly noticeable in the parietal region and in all of the occipital region except in the vicinity of the foramen magnum. In the region of the bregma the thickening was comparatively slight, but from that point forward the frontal bone showed increased thickening, which reached its maximum in the region of the glabella. No frontal sinuses were shown. The osteoplastic process was also marked throughout the whole floor of the anterior fossa of the skull, apparently involving the sphenoid bone, the maxilla and the malar bones but not the mandible. All of the bone forming the pituitary fossa had the same even opacity as the other thickened portions, although the clinoid processes were not much larger than normal.

The lack of the characteristic structural markings in the affected bone gave it a curiously uniform appearance not unlike that of poured plaster. Except for its wide distribution in the bones of the skull, the condition resembled closely osteitis fibrosa localisata, a form of osteitis deformans or Paget's disease.

All of the long bones of the extremities showed pathologic change. Most of them showed loss of trabeculation, with an increase of density which made many portions almost opaque, while other portions, especially in the regions of the metaphyses, showed irregular thinning, which gave a blotched or streaked appearance, the streaks running always in the low axis of the bone. The cortex was greatly diminished and sometimes almost indistinguishable The shafts were increased in width, having an irregularly swollen appearance; at the same time they were obviously weakened, for they showed deformities similar to those which

TABLE 2.—*Laboratory Findings for J. McK.*

Subject of Test	Results of Test	
	March 1937	September 1937
Urinalysis	Normal	Normal
Red blood count	4,200,000	.....
Hemoglobin	95%	.....
White blood cell count	7,100	.....
Polymorphonuclears	80%	.....
Lymphocytes	19%	.....
Monocytes	1%	.....
Wassermann reaction of blood	Negative	.....
Calcium per 100 cc. serum	9.6 mg.	10.3 mg.
Phosphorus per 100 cc. serum	3.8 mg.	4.1 mg.
Phosphatase	143 units	157.5 units
Cholesterol per 100 cc. blood (fasting)	348 mg.	195 mg.
Nonprotein nitrogen per 100 cc. blood	25 mg.	.....
Creatinine	1.5 mg.	.....
Basal metabolic rate (Benedict and Talbot)	127%	122%
Fat per 100 cc. blood (fasting)	.....	558 mg.
Dextrose tolerance		
Blood sugar during fasting	.....	87 mg.
½ hour later	.....	111 mg.
1 hour later	.....	125 mg.
2 hours later	.....	118 mg.
3 hours later	.....	93 mg.
Calcium balance with intake of 0.1 Gm. calcium daily	Daily negative calcium balance of 0.3228 Gm.; urinary excretion was 16% of total excretion	

occur with rickets wherever weight bearing comes into play. No definite cystic formation was shown in any of the bones. The femurs revealed the most marked changes. Their necks had a blotched type of osteoporosis, and coxa vera had developed; the shafts had a thinned cortex, loss of trabeculation, increased density and some irregular increases in thickness; the lower third of each femur showed marked irregular osteoporosis of a streaky type. The left femur was bowed outward; the right had a compound or S-shaped curve. The tibias and fibulas had most of the changes noted in the femurs but in less marked form. The right tibia had a slight S curve, while the left was almost straight. The net result of the curvatures in the lower limbs was genu valgum.

In the metacarpal bones the changes in osseous architecture were very unusual. There were irregular areas of osteoporosis with sides which tended to be straight rather than curved, some of the patches being roughly triangular and none of them circular.

Laboratory findings (table 2) of interest were the high cholesterol content of the blood during fasting and the increased basal metabolic rate.

A biopsy of the right femur was done because of the cystic changes in the bone and the high cholesterol value. At operation it was seen that the femur was much longer than usual for a child of 6 years and presented a rather spongy appearance. Dr. Erb described the gross specimen of bone as soft and spongy. Microscopically the material consisted of cancellous bone; this was composed of numerous delicate trabeculae of living bone surrounded by endosteum and showing an occasional osteoclast. The nuclei in the trabeculae stained well. Between the trabeculae were wide spaces filled by loose connective tissue, through which ran a goodly number of blood capillaries. No mitotic figures or inflammatory cells were seen. A careful search was made for foam cells, but none could be observed in sections stained with hematoxylin and eosin or with scarlet red, nor could any doubly refractile bodies be demonstrated by the use of crossed Nicol prisms. No true compact cortical bone was seen, and that immediately underneath the periosteum had the same loose structure as that in the center, where ordinarily the marrow cavity would have been. Toward one side of one of the sections was seen a small area of acellular, slightly vascular fatty marrow. Nothing of the nature of cystic formation could be seen. The periosteum consisted of dense, relatively acellular fibrous tissue lined on its inner surface by a zone of young cellular connective tissue similar to that filling the intertrabecular spaces, with which it was continuous.

The child was readmitted on September 8 with a fracture of the left femur. No further changes were noted in her condition. On this admission the laboratory findings (table 2) showed little change from previous ones. The outstanding difference was that the blood cholesterol value during fasting had dropped from 348 mg. to 195 mg. The calcium balance was tested because of the fracture. Union of the fracture was normal.

COMMENT

These 2 cases are clinically similar to that described by McCune and Bruch,[1] in which there were precocious puberty, yellow pigmentation of the skin and generalized fibrocystic changes in the skeleton.

In the cases reported there have been no consistent chemical data. In practically all cases the calcium content of the serum was normal or slightly increased. This was demonstrated in J. P., who had a calcium value of 9.2 to 12 mg. per hundred cubic centimeters of blood. The inorganic phosphorus content was practically normal in all cases, including the 2 reported here. Studies in our cases showed a negative calcium balance, but the percentage of calcium excreted in the urine was within normal limits, which made the diagnosis of hyperparathyroidism improbable. The plasma phosphatase activity was increased in all determinations, which indicated that active osseous change was still taking place. Because of this finding and because union of the bone took place readily, it appeared that there was no disturbance in the calcium and the phosphorus metabolism. Of interest in both of these cases was the definite increase in the basal metabolic rate; in addition, there was increase in the systolic blood pressure, with moderate increase in the pulse pressure. This suggested hyperactivity of the thyroid gland, except that there was no increase in pulse rate or clinical evi-

dence of hyperthyroidism. It was also noted that the last dextrose tolerance test on J. P. showed a decreased carbohydrate tolerance, which may occur in cases of hyperthyroidism or of hyperpituitarism as well as of diabetes. Of the 15 cases reported in the literature, in only 4 [3] was the cholesterol content of the blood determined. An increase in serum cholesterol content was found in the case of Snapper and Parisel; [2a] in the others cholesterol values were normal. In our two cases J. P. had a steady increase in her blood cholesterol content from a normal value of 174 mg. to 256 mg. per hundred cubic centimeters, whereas J. McK. had a cholesterol value of 348 mg. and, six months later, one of 195 mg. A cholesterol tolerance test was done; according to Bürger,[4] this should show cholesteremia in cases of xanthomatosis of the skin. In J. P. there was cholesteremia. Normally there is approximately twice as much blood fat as blood cholesterol. In the case of J. P. this relationship was disturbed; in the last determinations the blood cholesterol value during fasting was greater than the blood fat value during fasting. No determination of blood fat was done on J. McK. at the time her cholesterol content was 348 mg., but on her second admission the blood fat value during fasting was approximately three times greater than the cholesterol value. These findings were contrary to those associated with hyperthyroidism, the total fat and the cholesterol content of the blood tending to be reduced in the latter case.

From the chemical study of our cases it would appear that some disturbance in lipoid metabolism was occurring, either primary or secondary. Biopsy of bone should have confirmed the chemical findings, but microscopic examination of bone tended to make the clinical picture more confusing.

SUMMARY

Two cases are described in which a girl 6 years and one 10 years of age exhibited precocious puberty, yellow pigmentation of the skin and osteodystrophy, the last progressing to cystic formation which resulted in fractures and skeletal deformity. There were increase in the basal metabolic rate, increase in the blood pressure, disturbance in the lipoid metabolism and decrease in carbohydrate tolerance.

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3. McCune and Bruch.[1] Footnote 2a. McCune.[2b] Snapper and Parisel.[2g]

4. Bürger, M.: Verhandl. d. deutsch. Gesellsch. f. inn. Med. **43**:186, 1931.

ACUTE NICOTINE POISONING WITH FATAL OUTCOME IN A CHILD

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Although nicotine has been recognized as a poison for over three centuries, fatalities in children from the administration of this substance are of sufficient rarity to warrant a report of this case.

REPORT OF CASE

F. B., a Negro girl aged 8 years, was in good health when she was attacked by a Negro man one afternoon. Her cries for help brought neighbors to the scene, who found the man pouring some dark-colored fluid down her throat. In the excitement which followed, the bottle and the fluid were lost. The girl complained of feeling badly and lay down on the bed, dropping off to sleep. Soon she became nauseated. Several hours later a severe convulsion and fever developed. The family physician administered chloroform and a sedative. After the convulsion the child remained in a stupor, but she roused sufficiently at intervals to take a small amount of nourishment by mouth. Within the next twelve hours she had two more convulsions, and the stupor became more pronounced. She was seen again by the family physician, who administered morphine and advised hospital care.

Examination on her admission to the McLeod Infirmary showed a well nourished girl lying in a deep stupor. The temperature was 103 F. The respirations were rapid and shallow. The pulse rate was 120, but the rhythm was regular. There was no stiffness of the neck or spasm of the extremities. The pupils were contracted, but this might have been due to the narcotic. The tendon reflexes were sluggish. The mouth and throat gave no evidence of any burn. The rest of the general examination gave negative results. Examination of the blood showed a leukocyte count of 13,450, with the following differential count: polymorphonuclears, 82 per cent; lymphocytes, 9 per cent, and mononuclears, 9 per cent. Lumbar puncture was performed; the spinal fluid was under a pressure of 40 mm. of mercury. The fluid was clear but contained 169 cells (lymphocytes) per cubic millimeter. The smear and the subsequent culture of the spinal fluid were negative for any bacteria.

Having no indication as to the nature of the poison which had been administered, I could employ only symptomatic treatment. A 10 per cent solution of dextrose was given intravenously, coramine (a 25 per cent solution of pyridine betacarbonic acid diethylamine) was given as a stimulant, and chloral hydrate was used as a sedative. In spite of these measures the child grew progressively worse. The temperature rose to 104 F., where it stayed. The respirations became weaker and more rapid, as did the pulse. There were no further convulsions,

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but muscular twitchings were frequent. The pupils remained contracted. Forty-eight hours after admission to the hospital and seventy-two hours after the administration of the poison, the patient died.

At the request of the coroner, the stomach, kidneys and bladder and sections of the liver and of the small intestines were sent off for chemical examination. The only abnormalities noted at the autopsy were a few plastic adhesions around the upper part of the small intestine and an area of mild inflammation in the upper portion of the duodenum.

B. F. Robertson, state toxicologist, reported that "the examination indicated the presence of considerable nicotine sulfate in both the liver and the stomach. The preparation sold under the trade name of black leaf 40 contains 40 per cent nicotine sulfate; it is used as an insecticide for plants, animals and poultry. In order to confirm the chemical reactions found in the examination of the stomach, some black leaf 40 was procured from a drug store; the substance gave reactions similar to those noted in the stomach."

COMMENT

Nicotine is one of the most powerful and rapid poisons known to man, 6 mg. of the pure alkaloid being sufficient to cause death in a human being.[1] In the presence of a massive dose, death ensues within a few minutes. The poison is absorbed not only from the mouth and stomach but from the conjunctivas, urethra, vagina and rectum.[2]

The usual symptoms of acute nicotine poisoning are nausea, vomiting, sweating, vertigo, headache, dyspnea, stupor, convulsions, pupillary changes, diminished and then accelerated pulse rate and respiratory paralysis.[3] A subnormal temperature is usually present, although Deacon reported a case in which the temperature was 104 F.[4] He mentioned the additional symptoms of generalized erythema and diarrhea.

As one considers the case reported here, one finds two factors which do not fit into the usual picture of acute nicotine poisoning. First, the child lived for seventy-two hours after the administration of the poison. This length of time before death is unusual, but it was probably due to slow absorption of the alkaloid. The child had eaten a meal only a short

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1. Webster, R. W.: Legal Medicine and Toxicology, Philadelphia, W. B. Saunders Company, 1930.

2. Macht, D. I.: Toxicological Note on Nicotine, J. A. M. A. **89**:900 (Sept. 10) 1927.

3. Edgar, W. H.: Tobacco Poisoning, J. Roy. Nav. M. Serv. **10**:15 (Jan.) 1924. Franke, F. E., and Thomas, J. E.: Study of the Cause of Death in Experimental Nicotin Poisoning in Dogs, J. Pharmacol. & Exper. Therap. **48**:199 (June) 1933. Willis, H. W.: Acute Nicotine Poisoning: Report of a Case in a Child, J. Pediat. **10**:65 (Jan.) 1937. Webster.[1]

4. Deacon, J. N.: Poisoning by Tobacco Applied to the Skin, Brit. M. J. **2**:61 (July 10) 1926.

time before swallowing the poison. Second, the increase of cerebrospinal fluid pressure was accompanied by an increase of the cellular elements of the fluid. I find no mention of this evidence of meningeal irritation in cases reported elsewhere, but the omission may be due to the fact that lumbar punctures were not performed.

SUMMARY

A case of fatal acute nicotine poisoning in an 8 year old girl is reported.

DYSTONIA MUSCULORUM DEFORMANS

CLINICOPATHOLOGIC REPORT OF A CASE

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Motor restlessness in the form of incoordinated, unsystematized, grotesque uncontrollable movements occurs in a number of morbid conditions, such as Huntington's chorea, double athetosis, Sydenham's chorea, Wilson's lenticular degeneration, Strümpell-Westphal pseudosclerosis and dystonia musculorum deformans, also known as torsion spasm or lenticular dystonia.

The diagnosis of the aforementioned morbid conditions is not difficult if the patient is seen in the fully developed stage of the disease, but when he is seen in an early stage correct diagnosis is almost impossible. Especially is this true of dystonia musculorum deformans, or, as Flatau and Sterling [1] proposed to name it, progressive torsion spasm. Not only are the clinical manifestations of this disease obscure and misleading, but even the histologic changes are by no means definite or uniform and are therefore unconvincing. If one considers that reports on the histologic changes of dystonia musculorum deformans are scarce and for the most part pertain to cases in which the disease had lasted for decades or was not always typical and uncomplicated, one will have to concede that additional studies, both clinical and pathologic, especially of pure subacute dystonia in children, are imperative.

The results of clinical and pathologic observations of a case of typical dystonia musculorum deformans in a child form the subject of this contribution.

REPORT OF CASE

History.—The history embodies data given to us by the patient's parents and by Dr. Irene Sherman, who observed the child on several occasions.

A Jewish boy aged 6 years, born by normal delivery, was seen by one of us (G. B. H.) on July 18, 1935. About August 1934 he began to experience difficulties with his gait: he was unable to run as well as other children of his age, and sometimes instead of running he would progress backward or would try to

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1. Flatau, E., and Sterling, W.: Progressiver Torsionspasmus bei Kindern, Ztschr. f. d. ges. Neurol. u. Psychiat. **7**:586, 1911.

hold on to something (the baby's buggy, for instance). He did not cooperate in games with other children, as he was unable to keep up with them; he dragged his legs, fell frequently and perspired easily. The difficulties in gait grew progressively worse. Thus in February 1935 (about six months after the onset) when the boy was walking he had his arms outstretched as though to maintain balance, and the feet were held wide apart.

If he was sitting on the floor playing and was called to another room, he often crawled rather than walked, and when playing ball he had the ball thrown to him while he sat.

Examination (July 18, 1935).—The boy was well nourished and exhibited no signs of paresis, paralysis, disturbance of speech or involvement of the cranial nerves. The only anomaly was inability to walk. The patient dragged the left foot, which he could not put forward at will, for the muscles would become rigid, with the foot flexed and rotated inwardly, thus preventing him from proceeding. He had to wait for the muscles to relax. He could walk barefooted better than with shoes on, and in the supine position he could sometimes freely move the hips, knees and ankles. Passive movements of the lower extremities met with temporary resistance, for they would set up rigidity, especially in the left lower extremity. The patient could not relax the flexed left foot when asked to do so; the flexed foot would become even more flexed, a phenomenon emphasized by Hunt.[2] Even on attempts at passive extension of the foot, flexion would increase and could not be overcome. The foot would become inverted and would remain so for some time. No tremor, bizarre movements or other involuntary movements were present. The only anomaly was, as has been noted, that of walking, which was caused by hypertonicity of the muscles of the lower extremities associated with occasional relaxation. The boy was not able to handle a pen or pencil, though the upper extremities exhibited no rigidity or abnormal postures.

The tendon reflexes were present, but because of the attacks of hypertonicity they were difficult to obtain, even with reenforcement. Electrical examination elicited good faradic and galvanic responses, and the sensibility was normal throughout.

Course.—The patient was examined two months later (September) by Dr. Irene Sherman. In walking, the patient raised and lowered the pelvis excessively and required support. When he was standing, the pelvis had at times an abnormal inclination; the upper part of the trunk and the head were thrown back; there were lordosis, scoliosis and excessive protrusion of the abdomen and buttocks, and the weight was shifted to the right foot. When the child was sitting, all of this disappeared. The muscles were large; the left buttock was larger than the right, but the musculature lacked the firmness commensurate with the size of the muscles. The muscular power was good. The tendon reflexes were all present; abnormal reflexes were absent, and the sensibility was normal. The mental age according to the Stanford-Binet intelligence test was 6 years and 10 months; the chronologic age, 6 years and 4 months. The intelligence quotient of 108 indicated a high average ability. The boy preferred to use the left hand and was awkward with his hands in using a pencil.

When examined on Jan. 11, 1936, the boy could not walk unless supported and led; he could not even stand unsupported. In walking he would put one leg far forward; the other leg was kept back, and the body was bent almost double. When the child was in the recumbent posture, the muscles would relax, as has been stated, and the extremity, or part of it, could be freely moved.

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2. Hunt, J. R.: The Progressive Torsion Spasm of Childhood (Dystonia Musculorum Deformans), J. A. M. A. **67**:1430 (Nov. 11) 1916.

By April 4 the patient could not move even when led; he had to be carried. He exhibited definite spastic contractures of the extremities; he often fell off a chair and was hurt. The upper extremities became awkward, and the movements in the lower extremities became extremely limited. The reflexes became exaggerated, but there were no pathologic signs, such as those of Babinski, Rossolimo or Hoffmann. The flexion-extension movements in both lower extremities were resistive.

In August, according to information given by the patient's mother, he was unable to lie on his back because of severe spasmodic involuntary contractures of the dorsal muscles, but he was comfortable when he lay on his abdomen

In September there was rapid progression of the involuntary muscular movements, which extended to the shoulders and head; every muscle of the body was in perpetual motion.

In October the motor restlessness increased, and feeding became difficult. The movements were accompanied by pain in the muscles of the legs, which was sometimes so severe that it made the child cry out, and sodium amytal (3 grains [0.19 Gm.] administered every four hours) and other sedatives (morphine) had to be given, although they produced only transient relief.

During this month the child was removed to St. Francis Hospital, Evanston, where nitrogen monoxide and ether had to be administered to relieve the violent clonic contractions of the extremities, trunk and head. The movements were twisting, throwing and gesticulating, with torsion of the neck; they deprived the child of sleep. It was impossible for the patient to control himself or to hold still long enough to take the fluids he was begging for. Ether anesthesia was continued for twenty-five minutes and was followed by intravenous injection of 2 grains (0.13 Gm.) of sodium amytal.

The temperature, which was 103 F. on admission to the hospital (with a pulse rate of 172 and a respiratory rate of 40), rose eight hours later to 108 F.; about nine hours after admission the child suddenly died.

Laboratory Data.—The urine on admission was light amber, slightly cloudy and neutral; the specific gravity was 1.020; albumin, acetone and sugar were absent.

Examination of the blood showed a hemoglobin content of 85 per cent, 5,380,000 red cells and 10,820 white cells, of which 81 per cent were polymorphonuclears and 19 per cent lymphocytes.

Examination of the spinal fluid revealed 81.5 mg. of sugar per hundred cubic centimeters; there was no globulin.

Clinical Diagnosis.—The clinical picture was that of a disturbance in the muscle tone, with a combination of hypertonia and hypotonia: a mobile spasm, or what Oppenheim called dystonia.[3] When the muscular restlessness so characteristic of dystonia was not in evidence (setting in late in this case) the clinical picture remained obscure. A definite diagnosis of dystonia musculorum deformans was made only after the onset of the violent muscular contractions.

Necropsy (Dr. O. T. Schultz).—This was performed ten hours after death, and was confined to the cranial cavity.

Gross Observations: The body was slenderly built and fairly well nourished. Bloody frothy fluid had escaped from the mouth and the nostrils. The abdomen was sunken. The fingers of the right hand were flexed with the thumb inside

3. Oppenheim, H.: Ueber eine eigenartige Krampfkrankheit des kindlichen und jugendlichen Alters (Dysbasia lordotica progressiva, Dystonia musculorum deformans), Neurol. Centralbl. **30**:1091, 1911.

the fingers, which gave the hand a clawlike appearance. The feet were in extreme extension. The calves appeared slender and wasted in comparison with the thighs; each calf measured 21 cm., the left thigh 41 cm. and the right 40 cm. in the greatest circumference.

The scalp was thin, dry and closely attached to the skull. The calvarium was thin, measuring 2 to 3 mm. in thickness; in the anterior portion of the parietal

Fig. 1.—Nucleus ruber. The ganglion cell *b* is swollen and homogeneous; the scattered round bodies are oligodendrocytes, one of which almost invaded the base of the upper ganglion cell (*a*).

bones, on each side of the sagittal suture, was a shallow depression of the inner table, which was semitranslucent in an area about 1 cm. in diameter. The dura appeared normal and was rather firmly attached to the skull. There was no accumulation of subdural fluids. The pia-arachnoid was thin and transparent; the pial vessels were only moderately engorged. The brain was large, weighing

1,475 Gm.; it was symmetric and of normal consistency. The convolutions were numerous and somewhat flattened; the hypophysis appeared of normal size.

The brain was delivered to the laboratory on October 21 in a solution of formaldehyde, U. S. P. (10 per cent concentration). Gross sections (coronal) revealed no macroscopic changes in the basilar nerves or in the ventricles, which were not dilated.

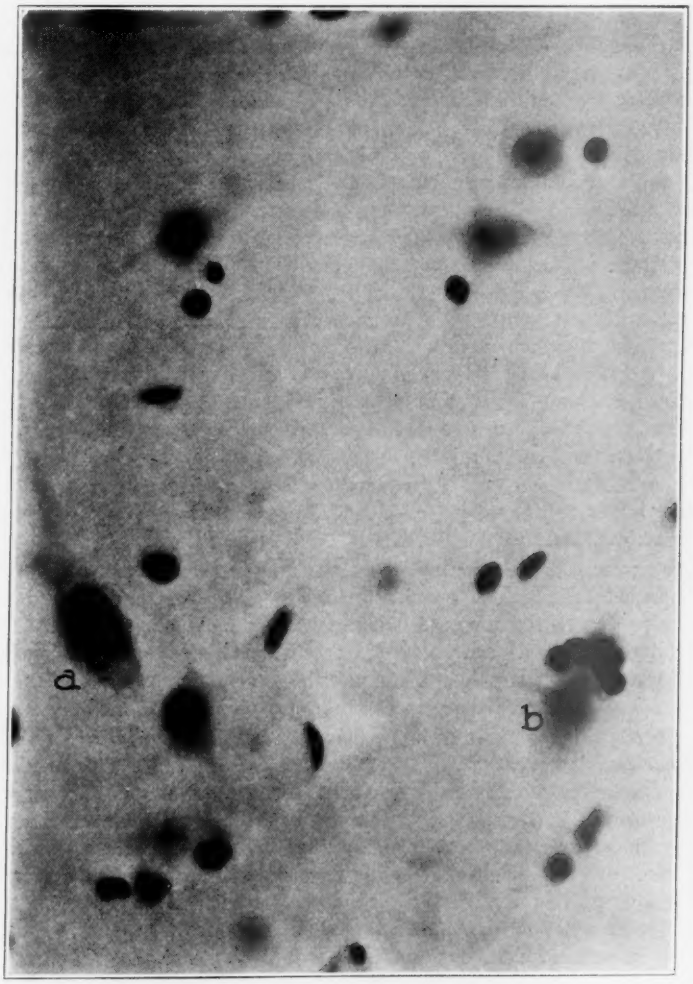

Fig. 2.—Caudate nucleus. The ganglion cells are pale and swollen, as is especially well seen in the cell *a*. The cell to the right (*b*) is invaded by neuronophages (oligodendrocytes). Toluidine blue stain was used.

Microscopic Observations: Pyroxylin sections of various areas of the cortex, basal ganglia, pons, medulla, cerebellum and uppermost portions of the spinal cord were stained with toluidine blue (for cells and nuclei) and by the modified methods of Weigert and Pal (for myelin fibers). Frozen sections from similar

regions were stained with scarlet red (for lipoids), with Bielschowsky's silver nitrate method (for neurofibrils), with Holzer's crystal violet stain (for glia), by the silver methods of Cajal and Hortega (for macroglia and microglia, respectively) and by the methods of Spielmeyer, Weil and Olivecrona (for myelin).

Especial attention was paid to the condition of the corpus striatum (putamen and nucleus caudatus) and to other parts of the so-called extrapyramidal system (globus pallidus, substantia nigra, corpus subthalamicum and nucleus ruber). In all the aforementioned regions, including the cortex and cerebellum, changes were found which were practically alike, differing from one another only in degree. The ganglion cells, including their axons and dendrites, which extended for a long distance, were swollen (figs. 1 and 2, *a*) and stained uniformly but poorly; their nuclei were for the most part well preserved but were pale and poor in chromatin, and many of the nucleoli were red. Nissl bodies were usually absent but occasionally appeared in the form of dust. Only few ganglion cells took the stain, but even those appeared homogeneous and without Nissl bodies (fig. 1, *b*). Some cells in the cortex were vacuolated and were often surrounded and invaded by oligodendrocytes; that is to say, they exhibited phenomena of satellitosis and neuronophagia (fig 1, *a*).

In the caudate nucleus, some ganglion cells, especially large ones, were represented only by their nuclei (which were devoid of chromatin granules and membranes) or by cells invaded by glial scavenger cells (neuronophages, fig. 2, *b*). Both large and small ganglion cells were equally affected. The small cells were often replaced by neuronophages or by deposits of calcium and were occasionally mixed with mast cells of huge size.

In the substantia nigra, some ganglion cells were well preserved; but the majority, including the axons and dendrites, were swollen. Neurofibrils could be demonstrated only in the dendrites.

In the putamen, the supraoptic nucleus and in the nucleus ruber some cells were liquefied (fig. 3) and broken up into badly stainable granular masses; the nuclei were hyperchromatic, which indicated beginning karyorrhexis. Such hopeless cellular changes as neuronophagia and liquefaction were not common. Less marked were the changes in the globus pallidus, and in the medulla the ganglion cells occasionally showed the presence of green pigment.

The predominating changes in the ganglion cells were swelling of their bodies and dendrites, degeneration of the Nissl bodies or their transformation into a dustlike substance (chromatolysis), hyperchromatosis of the nuclei (karyorrhexis) and occasionally homogenization of the entire cellular structure. Such changes were also more or less present in the cortical motor, temporal and parietal areas; there were rather mild changes in the pons, in the corpus subthalamicum, in the substantia nigra, in the olivary bodies of the medulla, in the nuclei of the bulbar nerves (tenth and twelfth) and in the supraoptic nucleus, the only component of the hypothalamus which was studied. Lipoid substances were occasionally in evidence as minute granules around the nuclei of the ganglion cells, but they were absent from the glia cells and from the perivascular spaces of the blood vessel walls. The white nerve substance stained poorly with the classic Kultschitzky-Pal method but stained much better with the methods of Spielmeyer, Weil and Olivecrona. It exhibited no such changes as degeneration of the myelin or axon.

As to the glia and the mesodermal tissues, the glia did not exhibit reactive changes, such as are seen in nerve degeneration. It was represented by the so-called oligodendroglia: naked glial nuclei (devoid of cytoplasm) which, like the nuclei of the ganglion cells, often exhibited breaking up of chromatin (karyorrhexis).

Astrocytes were only occasionally seen, while the microglia exhibited no changes whatever. The blood vessels showed no such changes as infiltration or proliferation of the endothelial or adventitial cells.

The pia was in general normal. Only around the cerebellum it was slightly hyperplastic and exhibited mesothelial cells, fibroblasts, lymphocytes and hyperemic blood vessels.

In the choroid plexus the tuft cells were swollen; their cytoplasm was homogeneous and occasionally contained small vacuoles; the blood vessels were immensely hyperemic.

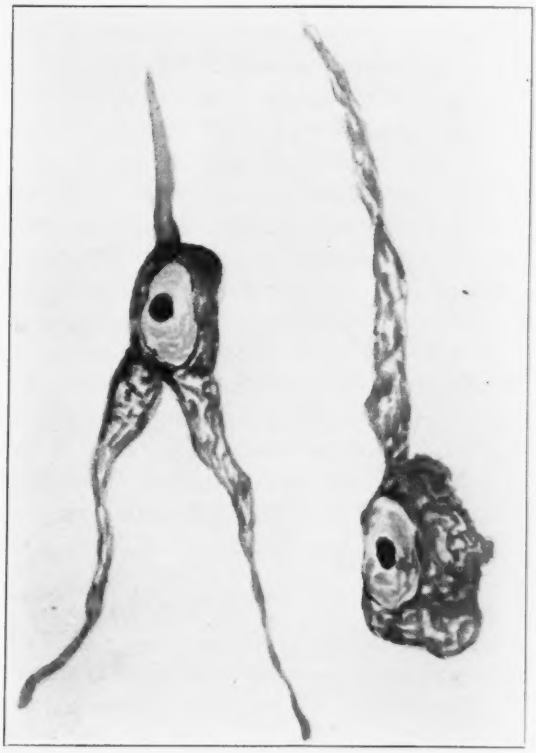

Fig. 3.—The cell to the left is from the putamen; that to the right, from the supraoptic nucleus of the hypothalamus; both are swollen and vacuolated, appearing liquefied (as described in the text).

The pituitary body was well developed. The eosinophils seemed to predominate; the basophilic cells seemed to be few, while the chromophobe cells were, as usual, gathered in clusters. Neither the eosinophilic nor the chromophobe cells transgressed the mesodermal rings, which traversed the tissues and exhibited no changes.

COMMENT

The changes in the brain substance which could be classified as acute cell disease of Nissl were universal, that is to say, they were not confined to the corpus striatum (caudate nucleus and putamen) but were present

in every other portion of the brain, including the cortex. In contrast, the clinical manifestations were not manifold, as one could expect from the widespread changes in the ganglion cells. For instance, there were no speech, sensory, visual, auditory or cranial nerve disturbances; there were no signs of paralysis or paresis. The only clinical manifestation was motor restlessness, which one would be tempted to ascribe to changes in the cells of the corpus striatum. However, equally severe cell changes, which were present elsewhere in the brain, did not elicit corresponding clinical signs, as has been noted. The distorted ganglion cells, at least the majority of them, as pictured in figures 1 and 2, were evidently capable of functioning. For this reason it is hardly justifiable to ascribe the motor restlessness, the manifestation of hypertonia and hypotonia, to the changes in the ganglion cells of the corpus striatum, of the nucleus ruber or of any other portion of the extrapyramidal system. The lesions were too diffuse even to suggest a local lesion; they denoted, as the changes showed (fig. 1 and 2), an acute or subacute process of only several weeks' or (probably) months' duration. Yet they were similar to the histologic changes in adults supposedly suffering from dystonia, in whom they lasted decades in some instances (cases of Thomalla,[4] Cassirer,[5] Davison and Goodhart,[6] Schmidt and Scholz [7] and others). It must be emphasized that in the majority of cases in which the condition was classified as dystonia neither the clinical nor the pathologic picture was that of real dystonia. Thus, in the cases of Thomalla [4] and Wimmer [8] the picture was that of Wilson's disease; in the cases of Divry and Evrard,[9] Guillain, Mollaret and Bertrand [10] and Munch-Petersen [11] it was that of chronic epidemic encephalitis; in Richter's case, [12]

4. Thomalla, K.: Ein Fall von Torsionspasmus mit Sektionsbefund und seine Beziehungen zur Athetose double, Wilsonschen Krankheit und Pseudosklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **41**:311, 1918.

5. Cassirer, R.: Halsmuskelkrampf und Torsionspasmus, Klin. Wchnschr. **1**: 53, 1922.

6. Davison, C., and Goodhart, S. P.: Dystonia Musculorum Deformans: A Clinicopathologic Study, Arch. Neurol. & Psychiat. (*a*) **29**:1108 (May) 1933; (*b*) **39**:939 (May) 1938.

7. Schmidt, W., and Scholz, W.: Klinischer und pathologisch-anatomischer Beitrag zur Torsionsdystonie, Deutsche Ztschr. f. Nervenh. **126**:53, 1932.

8. Wimmer, A.: Études sur les syndromes extra-pyramidaux; spasme de torsion progressif infantile (syndrome du corps strié), Rev. neurol. **37**:952, 1931.

9. Divry, P., and Evrard, E.: Spasme de torsion postencéphalitique: Étude anatomoclinique, J. belge de neurol. et de psychiat. **37**:179 (March) 1937.

10. Guillain, G.; Mollaret, P., and Bertrand, I.: Étude clinique, cinématographique et anatomo-pathologique d'un grand spasme de torsion postencéphalitique, Rev. neurol. **1**:342, 1934.

11. Munch-Petersen, C. J.: Beiträge zur Frage des pathologisch-anatomischen Substrats der Torsiondystonie, Acta psychiat. et neurol. **10**:391, 1935.

12. Richter, H.: Beiträge zur Klinik und pathologischen Anatomie der extrapyramidalen Bewegungsstörungen, Arch. f. Psychiat. **67**:226, 1923.

which is not considered by some to be a case of dystonia, the clinical picture was complicated by unilateral destruction of the pyramidal tract. Only the cases of Cassirer,[5] Davison and Goodhart,[6] Marinesco and Nicolesco [13] and Schmidt and Scholz [7] and another case of Wimmer [14] were instances of fairly pure, uncomplicated dystonia. But in all cases the disease occurred in adults, except in Wimmer's case, in which the malady lasted five years. The patient of Marinesco and Nicolesco [13] was 16 years old, and the disturbances lasted about ten months, less than in our patient, while Cassirer's patient presented clinically only partial dystonia (spasmodic torticollis). In all these cases, regardless of some discrepancies in the clinical picture, course and duration, the histologic changes were essentially like those in our case. The necrobiotic foci observed by Davison and Goodhart [6a] and the shrinkage and other changes in the putamen, with a diminished number of ganglion cells, as described by Richter [12] and by Davison and Goodhart [6] were not present in our case; this may have been due to the differences in the ages of the patients, those in the last-mentioned cases having been much older. Save for the severe involvement of the putamen and the glial changes, the pathologic picture in our case resembled that in the cases of Thomalla [4] and Wimmer,[8] which, as has been pointed out, were cases of Wilson's disease. One may thus state that Wilson's disease, chronic encephalitis and dystonia musculorum deformans may possess more or less similar pathologic features—those of acute cell disease of Nissl. In the case of Marinesco and Nicolesco,[13] which, as has been noted, was only of ten months' duration, the acute changes were associated with signs of chronic cell disease (cell sclerosis, mild glial reaction and reduced number of ganglion cells), which were invariably present in the cases of Richter [12] and Schmidt and Scholz [7] in which involvement was of long standing. Yet even in these cases of long duration the acute manifestations described in the present contribution were predominant and were not confined to the corpus striatum but were present throughout the brain. They were diffuse.

For the reasons mentioned, the changes described cannot be considered the cause of the postural changes and the muscular restlessness—the essential features of dystonia. Histologic changes even more pronounced than those here described may be present in any case of severe intoxication, infection or exhaustion without producing clinical features of dystonia. The histologic striatal changes outlined are thus not specific

13. Marinesco, G., and Nicolesco, M.: Un cas anatomo-clinique de dystonie contorsive spasmodique avec lésions du striatum et des centres sous-thalamiques, Rev. neurol. **1**:973, 1929.

14. Wimmer, A.: Étude sur les syndromes extra-pyramidaux: Spasme de torsion infantile débutant par crises d'hémispasmes toniques (Epilepsie striée), Rev. neurol. **2**:281, 1925.

for dystonia and do not justify the assumption that they are its cause. One should rather assume with Ascher [15] that dystonia may be associated with extrapyramidal signs, such as rigidity of the muscles of facial expression, exaggeration of the plastic tone and absence of associated movements.

The clinical manifestations, hypertonia and hypotonia with or without violent motor restlessness, may be purely physiologic—disturbance of muscle tone. Just as in epilepsy one is confronted with pronounced clinical manifestations, which have no definite anatomic seat, so in dystonia one is confronted with definite clinical manifestations which have no precise pathologic localization. At any rate, dystonia musculorum deformans so far cannot be classified as an organic nerve disorder in the sense in which multiple sclerosis, tabes dorsalis and encephalitis are so grouped. The majority of neurologists even do not consider dystonia a clinical entity but think it a syndrome, which may be observed with various degenerative and inflammatory morbid conditions, such as Wilson's disease, Strümpell-Westphal pseudosclerosis, double athetosis, chronic encephalitis, Huntington's disease and focal lesions of the brain; an instance of the last-mentioned disorder has been reported by van Bogaert (tuberculoma of the frontoparietal region).[16] True as this may be, the concurrence of hypertonia and hypotonia with torsion spasm is marked only in dystonia musculorum deformans, and even if some manifestations of the latter occur in other morbid conditions it should not be deprived of its autonomy. For instance, epilepsy in its most typical form occurs with tumors or syphilis of the brain, yet one would not deny the existence of epilepsy as a morbid entity. Like epilepsy, dystonia musculorum deformans is an independent morbid entity which is caused by some physiologic or metabolic changes in the musculature and possesses certain features which may permit an early diagnosis. In the presence of violent jerkings and muscular distortions, a diagnosis of dystonia is not difficult. When the main or the sole features are the disturbances of posture or gait, the progression backward and the inability to run or jump because of sudden and prolonged muscular spasms, the difficulties of diagnosis are usually immense. Thus, according to Mendel,[17] Oppenheim diagnosed the disease in his first case as Friedreich's ataxia combined with athetosis; Schwalbe and Ziehen [18] in

15. Ascher, E.: Die Torsionsdystonie im Kindesalter, Jahrb. f. Kinderh. **144**: 127, 1935.

16. van Bogaert, L.: Observations anatomiques et cliniques des spasmes de torsion, Rev. neurol. **1**:923, 1929.

17. Mendel, K.: Torsiondystonie (Dystonia musculorum deformans, Torsionspasmus), Monatschr. f. Psychiat. u. Neurol. **46**:309, 1919.

18. Ziehen, T.: Fall von tonischer Torsionsneurose, Neurol. Centralbl. **30**: 109, 1911.

their cases as "a peculiar tonic type of spasm with hysterical manifestations" or as "tonic torsion neurosis," and Patrick,[19] Wimmer and others, as hysteria, while in the case of our patient, who was seen by a number of clinicians, the diagnoses had been chronic encephalitis, hysteria, general tic (tic malady), dystasia-dysbasia, progressive muscular dystrophy and other conditions.

If one would bear in mind that modified types of dystonia musculorum deformans may occur, such as the spastic type of Hunt [2] and the spasms of attitude described by Guillain, Mollaret and Bertrand,[10] and that, as was stressed by Wechsler and Brock,[20] two forms of dystonia musculorum deformans (the myostatic and the myokinetic) may be differentiated, with predominance of the postural element in some cases and the kinetic in others, mistakes in the diagnosis would probably be fewer.

Whatever the type, the disease is not (as is almost universally believed) an organic nerve disease, though it may be a manifestation or complication of an organic disease process, as has already been emphasized. In its pure form, it may be included with the same group as Thomsen's disease, in which the main manifestations are also hypertonicity and absence of changes in the central nervous system. Because of the similarity, one of us (G. B. H.) in another case of typical dystonia musculorum deformans in a child administered chocolate-coated tablets of quinine sulfate (2 or 3 grains [0.13 or 0.19 Gm.] three times a day), with unexpected, very favorable results. This case is still under observation and will be recorded in due time.

SUMMARY AND CONCLUSIONS

A clinical and pathologic study of a comparatively recent case of dystonia musculorum deformans in a child is recorded.

The earliest manifestations were those of a functional nervous disorder.

There was absence of correlation between the extensity of the clinical and that of the pathologic manifestations.

The histologic changes were acute and diffuse; they occurred throughout the brain, including the cerebellum and the medulla, but were not typical of any known organic disorder of the central nervous system.

The extrapyramidal system (the corpus striatum, for instance) was affected in some portions probably more than any other part of the brain.

Dystonia is a definite morbid entity in which the main manifestation probably consists of anomalies of muscle tone, such as are seen with myotonia congenita; quinine therapy therefore should be tried.

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19. Patrick, H., in discussion on Hunt.[2]

20. Wechsler, I., and Brock, S.: Dystonia Musculorum Deformans, Arch. Neurol. & Psychiat. **8**:538 (Nov.) 1922.

Progress in Pediatrics

DISTURBANCES OF ROTATION OF THE INTESTINAL TRACT

CLINICAL PICTURE BASED ON OBSERVATIONS IN TWENTY CASES

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We have been interested in the clinical syndromes resulting from disturbances of rotation of the intestinal tract in the course of fetal development, in the recognition of these syndromes and in their surgical treatment. In this paper we shall discuss clinical problems which involve a single anatomic division of the alimentary tube, namely, the part derived from the midgut loop, or that portion of bowel which is supplied by the superior mesenteric artery; within this limited territory we shall ignore, save as they have occurred coincidentally or are concerned secondarily with differential diagnosis, all types of congenital malformation except those that have to do with disturbances of the process of intrauterine developmental rotation and subsequent fixation of the distal portion of the duodenum, the small intestine and the proximal portion of the colon.

NORMAL DEVELOPMENT OF THE INTESTINAL TUBE

It is incumbent on the pediatrician, as well as on the surgeon, to be familiar with the embryologic development of the digestive tube, so that he may be prepared to recognize its vagaries. Descriptions of the process of intestinal rotation are given in the articles of Frazer and Robbins,[1] Dott,[2] Hecker, Grünwald and Kuhlmann,[3] Haymond and

From the Babies Hospital and the Department of Diseases of Children and the Department of Surgery, Columbia University.

Dr. George H. Humphreys made several of the sketches which illustrate the case reports.

1. Frazer, J. E., and Robbins, R. H.: On the Factors Concerned in Causing Rotation of the Intestine in Man, J. Anat. & Physiol. **50**:75, 1915.

2. Dott, N. M.: Anomalies of Intestinal Rotation: Their Embryology and Surgical Aspects, with Report of Five Cases, Brit. J. Surg. **11**:251, 1923.

3. Hecker, P.; Grünwald, E., and Kuhlmann, J.: Les anomalies congénitales de forme et de position du gros intestin et leur importance chirurgicale, Rev. de chir. **64**:661, 1926.

Dragstedt,[4] Gardner and Hart [5] and Wakefield and Mayo.[6] In this difficult exposition, textbooks on embryology fall far short of these contributions to the surgical literature.

Frazer and Robbins [1] have divided the process of intestinal rotation into three stages: The first stage comprises the time during which the midgut loop occupies the umbilical cord, which lasts up to about the tenth week of intrauterine life. Starting as a short loop lying close to the midsagittal plane (fig. 1 *A*), the portion of the alimentary tube supplied by the superior mesenteric artery grows forward during this first stage, part of it leaving the abdominal cavity and entering the lumen of the umbilical cord. As it elongates farther, it turns about the artery, which serves as an axis (fig. 1 *B*), first through 90 and then through 180 degrees in a counterclockwise direction. Early in this stage the prearterial segment, comprising the jejunum and the upper part of the ileum, lies above and anterior to the artery, while the postarterial segment, which includes the lower portion of the ileum and the proximal portion of the colon as far as the middle of the transverse colon, lies below and posteriorly. The effect of rotation during this first stage is to reverse the positions of these two segments, the postarterial segment being brought into the forward and superior position.

The second stage demarcates the time interval during which the coils of gut recede from the umbilical cord (fig. 1 *C*) and return to the abdominal cavity, now sufficiently roomy to accommodate them; this stage is completed when the cecum reaches the right loin, at some time in the eleventh week (fig. 1 *D*). All authorities have agreed that this stage lasts but a short time, some believing that it may be a matter merely of minutes or even seconds. During the second stage, when the normal mechanism is in operation, the proximal coils of jejunum leave the umbilical cord first, passing from right to left behind the superior mesenteric artery and thus adding another 90 degrees of counterclockwise rotation, with the mesenteric vessels forming an axis. The first coils, those of the duodenojejunal junction, are pushed farther to the left by those that follow after, and succeeding coils are packed more and more to the right, so that the cecum and ascending colon, the last of the train, come to lie in the right hypochondrium. The duodeno-

4. Haymond, H. E., and Dragstedt, L. R.: Anomalies of Intestinal Rotation: A Review of the Literature with Report of Two Cases, Surg., Gynec. & Obst. **53**:316, 1931.

5. Gardner, C. E., Jr., and Hart, D.: Anomalies of Intestinal Rotation as a Cause of Intestinal Obstruction: Report of Two Personal Observations; Review of One Hundred and Three Reported Cases, Arch. Surg. **29**:942 (Dec.) 1934.

6. Wakefield, E. G., and Mayo, C. W.: Intestinal Obstruction Produced by Mesenteric Bands in Association with Failure of Intestinal Rotation, Arch. Surg. **33**:47 (July) 1936.

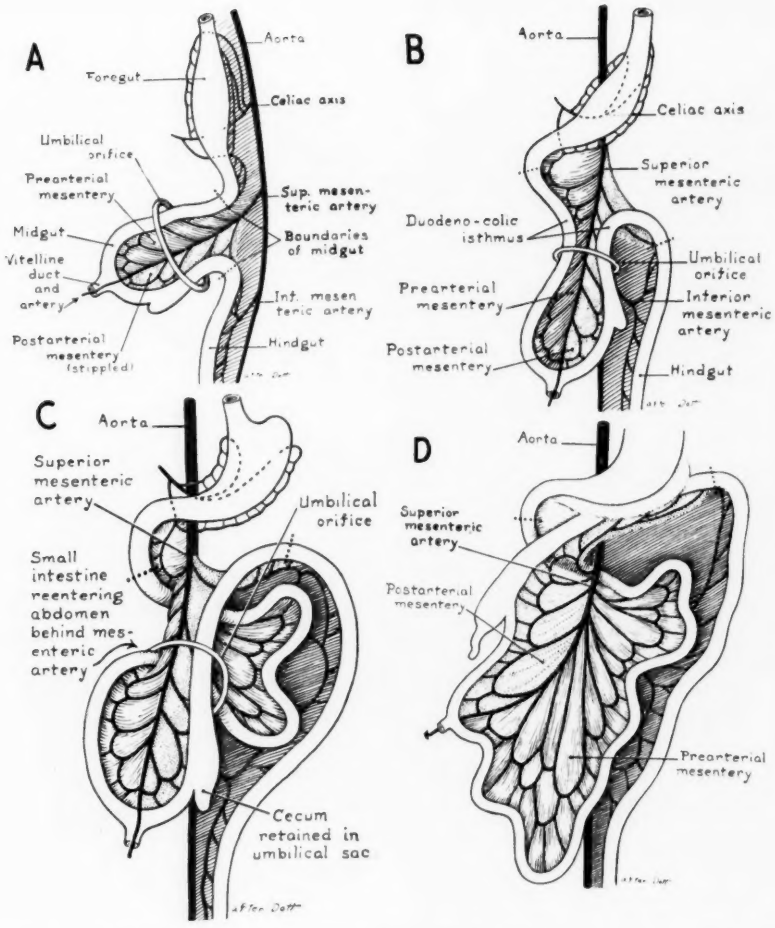

Fig. 1.—*A*, diagram of the alimentary tract at the fifth week of intrauterine life (lateral view). The foregut, midgut and hindgut are shown, with their individual supplies of blood supported by the common dorsal mesentery in the sagittal plane. The midgut loop has been extruded into the umbilical cord.

B, diagram of the alimentary tract at the eighth week of intrauterine life (anteroposterior view). The first stage of rotation is being completed. Note the narrow duodenocolic isthmus from which the midgut loop depends, the position of the small intestine on the right and that of the colon on the left. Maintenance of this arrangement within the abdomen after birth is spoken of as nonrotation.

C, diagram of the alimentary tract at about the tenth week, during the second stage of rotation (anteroposterior view). The bowel in the temporary umbilical hernia is in the process of reduction, the most proximal part of the prearterial segment entering the abdomen to the right of the superior mesenteric artery first and the remainder of the bowel following in orderly sequence. The superior mesenteric artery is held forward close to the abdominal wall by the cecum and the ascending colon, which permits the bowel to pass under them. As the coils of small intestine collect within the abdomen, the hindgut is displaced to the left and upward.

D, diagram showing the condition of the alimentary tract at the end of the second stage of rotation (eleventh week). From its original sagittal position the midgut has rotated 270 degrees in counterclockwise direction about the origin of the superior mesenteric artery. Figure 1 has been reproduced from an article by Gardner and Hart,[5] with the permission of the authors.

jejunal junction and the ileocecal junction are in this way wedged apart by the intervening loops of small intestine, and the "duodenocolic isthmus," the gap between these structures as measured on the posterior wall of the abdominal cavity by the mesenteric root of the small intestine, is effectually lengthened.

The third stage lasts from this time until shortly after birth. It is characterized by orderly fusion of portions of the mesentery of the midgut to the posterior parietal peritoneum, with resulting fixation of the duodenum, cecum and ascending colon and establishment of a broad linear base for the mesentery of the small intestine; this base extends from the duodenojejunal fossa on the left and above to the ileocecal junction to the right and below. During this third stage the cecum, as clearly demonstrated by Hunter,[7] does not "descend" into the right lower quadrant, as is so often stated, but remains in a fixed position with relation to the skeleton, while growth of the ascending colon and of the proximal portion of the transverse colon, accompanied by marked reduction in the relative size of the liver, eventually achieves the normal postnatal configuration of this portion of the large bowel. Fusion of the mesentery of the transverse colon with the greater omentum to form the gastrocolic ligament is an additional feature of the normal third stage.

ERRORS IN DEVELOPMENT OF THE INTESTINAL TUBE

The inherent capacity for error in this complicated process is so great that no explanation thus far offered for the avoidance of anomaly in the normal disposal of the organs seems adequate. If the return of the midgut loop from the umbilical cord fails to take place, the result is exomphalos, or congenital umbilical hernia, with the accompanying failure of normal counterclockwise intestinal rotation beyond the first stage of 90 degrees, the component parts of the midgut loop occupying the relative positions which obtain at about the tenth week of gestation. *Failure of rotation* during the second stage may occur independently of exomphalos, however, the coils returning from the umbilical cord to the abdominal cavity en masse and retaining their primitive arrangement, with the jejunum and ileum on the right, the entire large intestine on the left and the ileum entering the cecum from right to left. Usually there is an accompanying sharp duodenal kink at the junction of the second and the third portion or at the duodenojejunal flexure. When the failure of rotation is incomplete in degree (as is more commonly the case), so that the intestines have a pattern intermediate between nonrotation and the normal postnatal disposition, the condition is

7. Hunter, R. H.: A Note on the Development of the Ascending Colon, J. Anat. **62**:297, 1928.

spoken of as *malrotation*. If the caudal (postarterial) segment of the midgut precedes the cephalad (prearterial) segment in its return from the umbilical cord to the abdominal cavity, *reversed rotation* is the usual outcome: The cecal portion of the midgut loop, taking the lead, passes behind the superior mesenteric artery from left to right in leaving the umbilical cord, so that the normal counterclockwise rotation of the entire midgut loop is unwound and replaced by a final clockwise rotation of 90 degrees, the transverse colon coming to lie behind the duodenum. Other and much more uncommon errors of the process of return of the midgut loop to the abdominal cavity have been reported, such as the imprisonment of coils of the jejunum and of the upper portion of the ileum in a ballooned out pouch of mesentery of the lower portion of the ileum or the herniation of coils of small intestine through an opening in the mesentery or into the lesser peritoneal cavity.

But while many of these anomalies of the second stage of rotation cause no immediate obstruction of the alimentary tube, they have this one threat in common: Errors of the first or second stage of rotation are liable to disrupt the normal development of the intestinal attachment at subsequent stages and in this way indirectly to bring on symptoms of ileus after the burden of digestion is assumed. Thus failure of the mesenteric root of the small intestine to be spread out in a long diagonal base line on the posterior abdominal wall carries with it the risk of volvulus; for when the duodenocolic isthmus retains its primitive shortness and the pedicle of the mesentery of the midgut loop remains narrow—that is, when the duodenojejunal junction is situated close to the ileocecal junction—it is relatively easy for the whole mass to twist about the axis of its pedicle. Failure of the cecum and ascending colon to become attached to the posterolateral aspect of the abdominal parietes, allowing the cecum alone (cecum mobile) or the cecum and the ascending colon (mesenterium commune) to swing free on an extension of the ileal mesentery, may likewise produce susceptibility to volvulus in this portion of the gut. In association with any of these anomalies of rotation, there is increased likelihood of the persistence of abnormal peritoneal bands, especially in the region of the duodenum (Clausen [8] has described this as hyperfixation), so that the lumen of this portion of the digestive tube is compromised by compression or kinking. Congenital peritoneal "adhesions" are more frequently related to the developmental process of fusion than to a presumed intrauterine inflammation.[9]

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8. Clausen, S. W.: Persistent Vomiting in Early Life, New York State J. Med. **38**:110, 1938.

9. Huntington, G. S.: The Anatomy of the Human Peritoneum and Abdominal Cavity Considered from the Standpoint of Development and Comparative Anatomy, Philadelphia, Lea Bros. & Co., 1903.

MATERIAL

We have assembled 20 cases in which disturbance in the process of intestinal rotation gave rise to clinical symptoms. In 18 of these the anatomic abnormality was visualized at operation. In the other 2 cases the clinical syndrome of partial duodenal obstruction was associated with roentgen evidence of incomplete rotation, which afforded a reasonable presumption that the two conditions were causally related. Both of these patients were kept under close observation for several weeks, during which they gradually improved without operative intervention. The probable mechanism of this temporary block will be discussed later. All of the 20 patients save 1 presented symptoms of obstruction of the alimentary tube; in the 1 exceptional case the outstanding complaint was melena, which was found to be caused by blocking of the venous return at the root of the mesentery of the small intestine.

For presentation and discussion we have arranged these cases according to the immediate anatomic cause of obstructive symptoms. We have not found it possible, on the basis of clinical and roentgen evidence, to predict the exact abnormality that will be found in a given case, and we chose this mode of presentation partly to bring out the statistical probabilities involved in our experience with anomalies of rotation and partly to emphasize the wide range of possibilities.

MALROTATION WITH VOLVULUS OF THE PORTION OF INTESTINE ARISING FROM THE MIDGUT

The largest single group is that in which volvulus of the part of the intestine derived from the midgut loop occurred; in the first 6 cases there was no other cause of obstruction. In most instances the entire small intestine was involved in the twist. We have arranged the cases in the order of age at operation.

CASE 1.—Andrew G. began vomiting when first put to breast and continued to vomit bile-stained material until brought to the hospital, on the day after birth. He was seriously ill, with shallow, grunting, moderately rapid respirations. The abdomen was distended, especially in the upper part, where the percussion note was tympanitic; the right flank was a little fuller than the left. Brick-red meconium was passed. Chvostek's sign was present. A plain roentgenogram (fig. 2 *A*) apparently showed fluid levels in both sagittal and transverse projections, the presence of gas in the small intestine suggesting that the obstruction was not complete. It was hoped that further study with a radiopaque meal would give more precise information on this point, but the patient rapidly became worse. On the following day, two days after birth, operation was performed.

The peritoneal cavity was filled with dark bloody fluid, and all of the loops of small intestine were distended, dark red and almost black, with the serosa broken in several places. Clinically, the intestine appeared gangrenous. Its loops were so tightly bound down that it was impossible to deliver them outside of the abdomen, and the wound was closed without further operative procedure.

The patient died about eight hours after operation. Autopsy showed volvulus of the entire small intestine (fig. 2 *B*). The cecum, incompletely rotated and attached to a long mesentery, was firmly bound in the midline by the turns of the mesenteric root and by the overlying mass of small bowel. There was a large quantity of free

dark blood in the peritoneal cavity; all of the abdominal organs were stained with it but were otherwise normal. The intestine showed deep congestion and dark purplish discoloration but microscopically was not gangrenous. In the upper lobe of the right lung there was early patchy lobular pneumonia.

Whether the volvulus in this case existed before birth is open to question. The unusual color of the meconium may perhaps suggest it, but further study of this evidence was not carried out, since the patient's condition, which required immediate surgical intervention, was of such grave concern. Admittedly, earlier operation might have improved the chance of survival; but the urgency of the situation was not appreciated

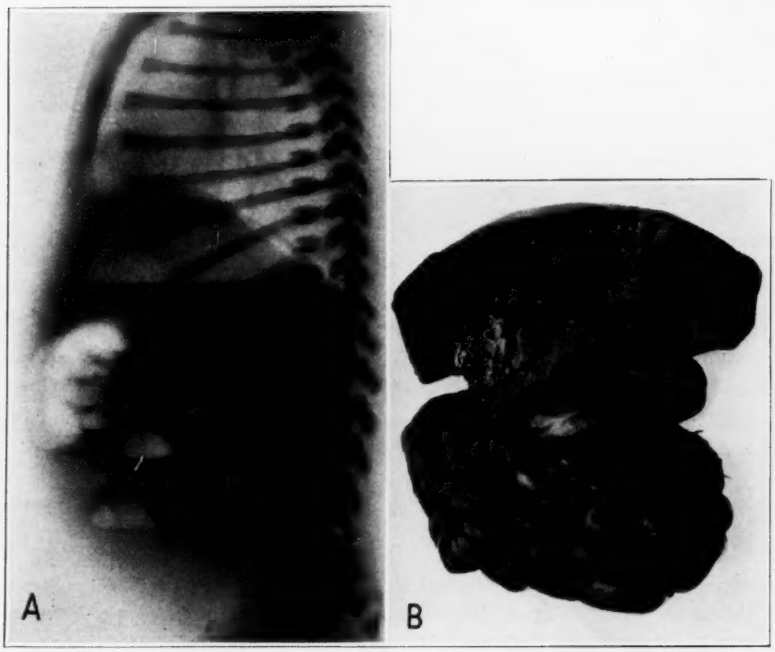

Fig. 2 (case 1).—*A*, lateral roentgenogram showing gas shadows and fluid levels. *B*, liver, stomach and intestine, removed en bloc. There is clockwise volvulus of the intestine about the root of its mesentery.

and, in fact, was not in keeping with our other experiences with this type of lesion. It is important to point out, in connection with this case, that the encroachment on the lumen of the intestine was sufficient to produce the clinical picture of high intestinal obstruction but insufficient to prevent gaseous distention of the bowel below the point of narrowing, while at the same time there was enough damming back of the venous return to flood the peritoneal cavity and the lumen of the bowel with blood and to produce intramural intestinal hemorrhages.

CASE 2.—Bettina D., an infant who was large at birth, was not nursed but was given at once a formula of milk, water and corn sirup. Projectile vomiting of bile-stained material followed the first feeding and continued until her admission to the hospital. After the passage of normal meconium, the stools became constipated. Roentgen studies made at the age of 5 days showed incomplete obstruction at the third portion of the duodenum, with gastric retention of more than 90 per cent of the ingested material at three hours. The abdomen was prominent but soft; no waves were seen, and no pyloric tumor was felt. The leukocyte count was 31,000 per cubic millimeter, with 71 per cent polymorphonuclears.

At operation at the age of 5 days, there was found volvulus of the lower portion of the ileum, with one and a half turns in a clockwise direction. The cecum and appendix lay in the left upper quadrant, and there was no fusion between the transverse mesocolon and the gastrocolic omentum. The volvulus was reduced without difficulty, and the cecum was sutured to the parietal peritoneum in the right lower quadrant with interrupted sutures of chromic catgut.

On the day after operation the temperature rose to 101.4 F., and there was some abdominal discomfort and vomiting; this was relieved by lavage, with recovery of about 60 cc. of thick green mucus containing curds and small flecks of blood. Thereafter convalescence was uneventful, the caloric content of feedings being raised gradually. During the second week after operation the stools became normal in number and volume. Six months after discharge the patient was reported to be entirely well.

The pathologic condition found at operation in this case was typical of malrotation with volvulus, except that it is unusual to have so small a segment of the intestine as the lower portion of the ileum alone involved. Lack of fusion between the transverse mesocolon and the gastrocolic omentum is the rule in such cases, as has been pointed out in many published reports; this affords the surgeon an immediate and direct indication of developmental disturbance as the underlying cause.

CASE 3.—Annie G. had bilious vomiting on the day after birth, and this symptom became progressively more dominant. Continuing loss of weight, the passage of infrequent small green stools and transient fever due to dehydration led to her admission to the Babies Hospital at the age of 6 days. Gastric peristaltic waves and projectile vomiting were seen, and three observers felt a pyloric mass contract and relax under the finger; but the presence of bile in the vomitus established the site of obstruction below the ampulla of Vater. A barium sulfate meal was seen to pass through the stomach almost immediately, visualizing a markedly dilated duodenum as far as the third portion, where practically complete obstruction was encountered. At the end of one hour only a few flakes of barium sulfate were seen scattered throughout the upper part of the small intestine. Questionable Chvostek, peroneal and Trousseau signs were obtained. The serum chloride level was 81 millimols per liter and the bicarbonate level 28 millimols. Twenty-four hours were devoted to restoring the fluid and the electrolyte balance.

Operation was performed at the age of 7 days. The jejunum was twisted one full turn in clockwise direction about the mesenteric root (fig. 3). The cecum lay in the right upper quadrant, and above the base of the mesenteric root the duodenum was greatly dilated. After the volvulus had been reduced, the abdominal wall was closed without any attempt to attach the cecum to its normal bed.

Convalescence was uneventful except for mild superficial infection of the wound. At 10 months of age the patient weighed 20¼ pounds (9,185 Gm.), and at 16 months, 24½ pounds (11,113 Gm.). She was free from digestive disturbance.

A pyloric mass was palpated in this case, as in cases 5 and 9. A similar phenomenon has been observed in other types of duodenal obstruction, notably in cases of developmental atresia. In all probability the swelling represents the distended first portion of the duodenum itself, the tension in which fluctuates as the pressure within the lumen is raised by transmission of the impulse of a gastric peristaltic wave through the pyloric opening or is lowered when the wave reaches the pylorus, the duodenum thus imitating in a way the contraction and relaxation of

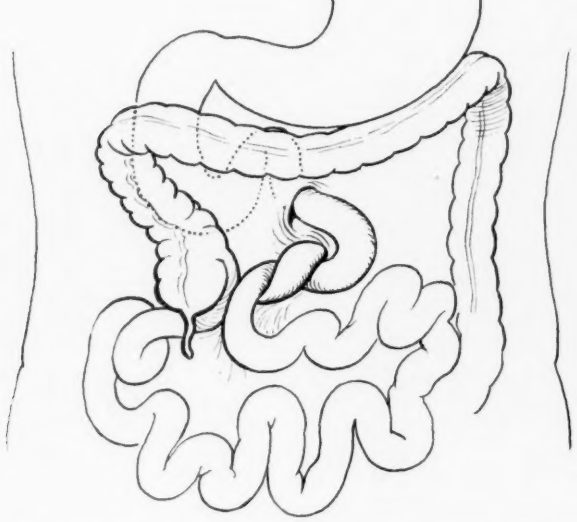

Fig. 3 (case 3).—Volvulus of the small intestine causing duodenal obstruction at the base of the mesenteric root.

the pyloric muscle itself. One would expect to identify true hypertrophic stenosis of the pylorus by the smaller size and firmer consistence of the mass and by the fact that it softens during relaxation without entirely vanishing; yet one must admit that the distinction is not always easily made by palpation alone, without taking into account the circumstance that the presence of bile in the vomitus points strongly to the location of the obstruction below the ampulla of Vater. In all of the cases in this series the pylorus itself, when examined at operation, was normal.

Case 4.—Beverly R. vomited bile-stained material on the day of birth, when first put to breast. Stools were infrequent, small and green. Weaning and various

changes of formula brought about no improvement, and the infant was admitted to the hospital at the age of 10 days. She was small and dehydrated, and the skin was ashen. The abdomen was scaphoid, with visible intestinal patterns. The non-protein nitrogen level of the blood was 76 mg. per hundred cubic centimeters. Two days after admission fluoroscopic study demonstrated dilatation of the stomach, with patency of the pylorus (fig. 4). At about the junction of the second and third portions of the duodenum an apparently complete obstruction persisted for five hours of observation.

After measures had been taken to restore the water and electrolyte balance, operation was performed, at the age of 12 days. There was no fusion between the gastrocolic omentum and the transverse mesocolon. The entire small intestine was found twisted through four full turns in a clockwise direction around the

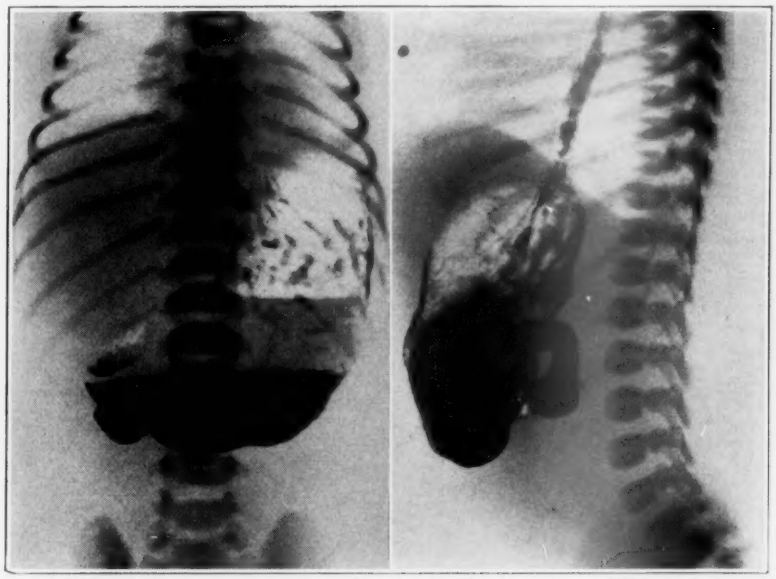

Fig. 4 (case 4).—Posteroanterior and lateral roentgenograms taken one-half hour after ingestion of an opaque meal. There is complete duodenal obstruction with dilatation of the stomach and duodenum.

root of the mesentery (fig. 5). The cecum and the ascending colon, which lay in the left upper quadrant, were brought down to their normal bed and sutured there.

Convalescence was slow. In spite of cautious progressive restoration of the caloric intake, vomiting returned nine days after operation, requiring further dietary restriction. It was eventually brought under control, and the stools became more voluminous. About four weeks after operation the patient's weight began to increase satisfactorily, and at the age of 8 weeks she was discharged. At 3 months she was reported to be doing well, but no information on her subsequent course is available.

Of the two modes by which volvulus produces symptoms, obstruction of the alimentary channel and circulatory block, the former is

obviously of more benign immediate import. Up to a point, even severe starvation is remediable. Just why a patient will exhibit a predominance of one type of symptom over the other is impossible to state. In this case obstruction of the alimentary lumen was present for twelve days and was known to be complete, or virtually so, by the tenth day; yet there was no bleeding into the bowel or into the peritoneal cavity, and at the time of operation the degree of engorgement of the intestinal circulation was only moderate, in spite of volvulus of 1,440 degrees. The extent of axial rotation of the involved loop about its mesenteric attachment is manifestly not the prime factor which jeopardizes the viability of the tissues.

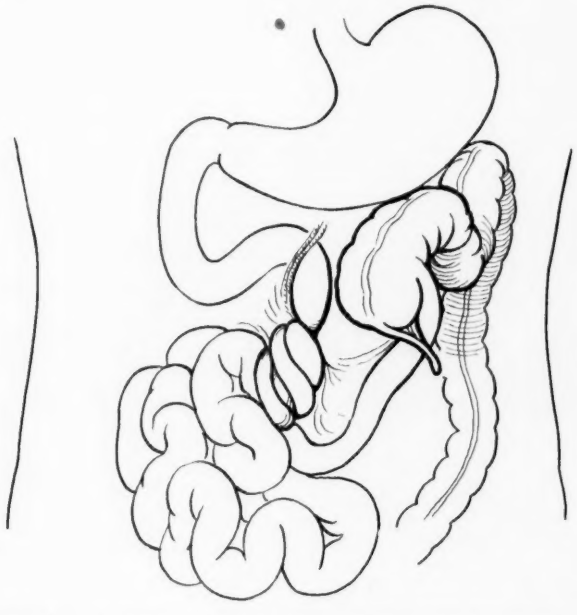

Fig. 5 (case 4).—Volvulus of the small intestine, with four complete turns of the mesenteric root causing obstruction at the duodenojejunal junction.

CASE 5.—Dorothy R. commenced vomiting on the day after birth and continued to do so with increasing persistence. From the start the vomitus was bile stained, and at times it was ejected in a projectile manner. Stools numbered two a day and were yellow. The child's weight, which was 3,510 Gm. at birth, had fallen to 2,760 Gm. by the time of admission to the hospital, at the age of 12 days. Gastric peristaltic waves were observed, and a pyloric mass was felt.

Operation was performed at the age of 14 days. The entire portion of intestine derived from the midgut loop, including the proximal portion of the large intestine, was twisted in a clockwise direction about the axis of the mesenteric pedicle (fig. 6). The volvulus was reduced, but no attempt was made to establish fixation of the cecum and the ascending colon.

Convalescence was satisfactory, and the patient was discharged at the age of 25 days, weighing 3,150 Gm.

Bilious vomiting recurred when the child was 1½ months old, and she was readmitted to the hospital weighing only 3,160 Gm. At the second operation a type of volvulus almost identical with the first was found, and the operative procedure was the same. The patient remained in the hospital for forty-seven days; she weighed 4,365 Gm. on discharge, at the age of 3 months.

At the age of 4½ years she was free from symptoms, and roentgen examination of the gastrointestinal tract showed nothing abnormal immediately after ingestion of the barium sulfate meal or twenty-four hours later. At the age of 5 years and 8 months the girl was again admitted to the hospital because of vomiting of three days' duration. Except for moderate ketosis and dehydration there were no abnormal physical findings, and the patient recovered promptly under conservative treatment.

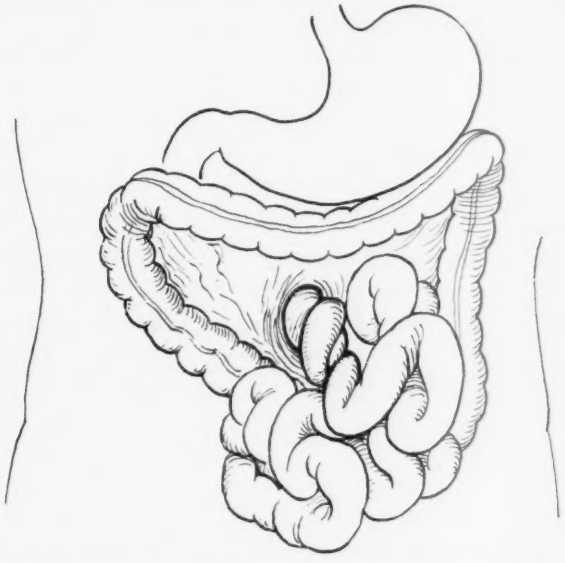

Fig. 6 (case 5).—Volvulus of the entire section of intestine derived from the midgut loop, as found at the first operation.

Her weight on discharge was 26.25 Kg. Similar attacks of vomiting, later associated with pain in the upper part of the abdomen and constipation, required hospitalization on four subsequent occasions, the last at the age of 10½ years. There were milder and more transitory attacks, which were treated at home. In spite of these episodes, the child's growth and development were normal. At one of these admissions to the hospital roentgen examination was repeated; in the films taken half an hour and one hour after the ingestion of barium sulfate it was noted that most of the barium sulfate–containing loops of jejunum and of the upper part of the ileum lay in the right half of the abdomen and that one long loop of the terminal part of the ileum coursed upward across the abdomen from left to right to join the cecum in the right upper quadrant. There was practically no ascending colon, the cecum leading almost directly to the transverse colon. The patient was last seen at the age of 14½ years; at that time she weighed 65.45 Kg. She had suffered no serious digestive upset since her last admission.

This is our only example of proved recurrence of volvulus of the section of intestine derived from the midgut loop. Several authorities have advised that the cecum be sutured to the posterior abdominal wall in the right lower quadrant in order that its abnormal mobility may be destroyed and the chances of recurrence of volvulus may thus be minimized. On the other hand, it is usually impossible to effect a restoration of the normal relationships without leaving a pocket behind the cecal mesentery in which a loop of bowel may subsequently become caught. We have tried both methods. In the case just described, in which nothing was done at the first operation except to reduce the volvulus, there was proved recurrence of the condition after one month, and probably there have been temporary recurrences since that time. Brenner,[10] Ladd [11] and Rosenblatt [12] reported similar experiences. We know of no instance in which volvulus was proved to have resulted from an attempt at cecal fixation. On the other hand, our experience in this respect is inadequate to justify our expressing a categoric recommendation.

The patient's experience during infancy prompts one to infer that the attacks of bilious vomiting which recurred at intervals throughout childhood and which came to be associated with constipation and with severe pain in the upper part of the abdomen were also attributable to recurrence of volvulus. The predisposing anatomic abnormality of the mesenteric attachment had not been intentionally corrected at either of her operations, so that the stage was constantly set for recurrence. Moreover, the ease with which the volvulus was reduced by direct surgical intervention lends support to the supposition that the twist might right itself under favorable circumstances. Unless a mild inflammatory process has immobilized the intestine to some extent, one cannot feel entirely reassured about this patient's future; in other words, it is possible that she may at some later date experience recurrence which will demand surgical correction.

Additional support for the inference that these milder attacks of vomiting and abdominal pain were attributable to the development and spontaneous resolution of volvulus of the part of the intestine derived from the midgut is derived from the circumstance that on each occasion when the patient was admitted to the hospital, care was taken to verify the absence of a precipitating factor, such as accompanying infection, dietary indiscretion, fatigue or emotional strain. The girl was of a

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10. Brenner, E. C.: Total Volvulus, Am. J. Surg. **16**:34, 1932.

11. Ladd, W. E.: Congenital Obstruction of the Small Intestine, J. A. M. A. **101**:1453 (Nov. 4) 1933.

12. Rosenblatt, M. S.: Faulty Rotation of the Intestines, Northwest Med. **36**: 425, 1937.

placid, passive disposition and was not considered allergic. Her attacks of "periodic vomiting" began without warning. The patient to be described in the report of case 19 presented a comparable picture of recurrent attacks of bilious vomiting, pain in the upper part of the abdomen and constipation, and during his last attack volvulus was found and was corrected surgically. The inclination of his parents to ascribe previous attacks to fatigue, excitement, dietary indiscretion or the ingestion of specific foods to which he was believed to be hypersensitive undoubtedly reflects an element of mental suggestion imposed by the medical profession; the boy's favorable course after operation dispels almost all doubt of the relation of recurring organic intestinal obstruction to the attacks of symptoms. Poynton,[13] Jacobi,[14] Camera,[15] Oehlecker,[16] Belot, de Vulpian and Millot,[17] King [18] and Koszler [19] mentioned a comparable theory of recurring and spontaneously resolving volvulus. Liebe,[20] although he wrote on "chronic volvulus," made it clear in his discussion that in the symptom-free intervals the volvulus was believed to have reduced itself. In addition, the literature on disturbances of intestinal rotation contains numerous examples of patients who in the past showed recurrent attacks of vomiting and other symptoms of obstruction which were variously interpreted as being due to indigestion, gastritis, periodic vomiting and similar conditions but who at operation or autopsy in childhood or even in adult life exhibited malrotation with volvulus of the part of the intestine derived from the midgut: for example, the cases of Janker (second case),[21] Mole,[22] Haymond and Dragstedt (first

13. Poynton, F. J.: Acetonaemia and Volvulus of the Small Intestine in Childhood, Lancet **1**:1045, 1924.

14. Jacobi, W.: Zur Frage des rekurrierenden Erbrechens mit Acetonämie, Arch. f. Kinderh. **83**:215, 1928.

15. Camera, U.: La base anatomique des vomissements cycliques réside-t-elle en une sténose extrinsèque congénitale du duodénum? Arch. de méd. d. enf. **33**: 583, 1930.

16. Oehlecker, F.: Dünndarmvolvulus bei teilweisem Situs inversus, Beitr. z. klin. Chir. **158**:515, 1933.

17. Belot, P.; de Vulpian, P., and Millot, J. L.: Un cas de défaut d'inversion du mésentère commun, Ann. d'anat. **11**:926, 1934.

18. King, E. S. J.: Two Uncommon Forms of Intestinal Obstruction Occurring Consecutively: Compound Volvulus and Retroposition of the Transverse Colon, Brit. J. Surg. **24**:817, 1937.

19. Koszler, V.: Zur Klinik des Mesenterium commune, Arch. f. Kinderh. **110**: 166, 1937.

20. Liebe, S.: Ueber chronischen Volvulus, Monatschr. f. Kinderh. **61**:436, 1935.

21. Janker, R.: Ein Beitrag zur Frage des Mesenterium ileocolicum commune, München. med. Wchnschr. **74**:192, 1927.

22. Mole, R. H.: Congenital Non-Rotation of the Intestine, Brit. J. Surg. **17**:670, 1930.

case),[4] Gardner and Hart (first case) [5] and Dixon and Deuterman.[23] Spontaneous correction is favored also by the rarity of visceral peritonitis and of other manifestations of a complicating inflammatory process in the patients coming to operation and by the retention of normal viability of the intestine even after many days of obstructive symptoms.

That periodic attacks of symptoms of high intestinal obstruction may occur in association with errors of rotation of the gut but independently of complicating volvulus has been made abundantly clear by Waugh,[24] Miller and Gage,[25] Weinbren and McGregor [26] and others; but in the presence of a constant obstructing factor, such as peritoneal bands compressing the duodenum or holding it in a kinked configuration, the symptoms are likely to be more chronic than intermittent, and the symptom-free intervals are not entirely clear. The patient is more or less constantly aware of vague abdominal discomfort, is unable to eat a full meal without distress and often suffers from chronic malnutrition. Jones and Morton [27] offered the explanation that under these conditions, when periodic attacks are superimposed on a background of marginal disturbance, spontaneous recovery from an acute episode depends on decompression of the bowel above the point of obstruction by the patient's violent vomiting.

CASE 6.—Charles W. refused to nurse during the first two days of life and later vomited bile-stained material forcibly. At the age of 3 weeks, when he was put on a formula, the vomiting diminished; he did well until the age of 4 months, when bilious vomiting returned in association with constipation. He was admitted to the Babies Hospital at the age of 4½ months; at that time he weighed 4,580 Gm. and was moderately dehydrated, with dehydration fever. He acted as if he were hungry. Gastric peristaltic waves were observed, but no pyloric mass could be felt. Bilious vomiting occurred as soon as feedings were begun in the hospital but then ceased for a few days. Roentgen examination (fig. 7) showed the stomach to be dilated. The upper part of the duodenum filled immediately, but during the first three hours of observation no part of the meal passed an obstruction at the junction of its second and third portions. At eighteen hours only a small amount of barium sulfate had progressed to the small intestine.

The patient was operated on twelve days after admission. No fusion was found between the gastrocolic omentum and the transverse mesocolon. The

23. Dixon, C. F., and Deuterman, J. L.: Malrotation of the Intestine, Proc. Staff Meet., Mayo Clin. **11**:140, 1936.

24. Waugh, G. E.: Congenital Malformations of the Mesentery: A Clinical Entity, Brit. J. Surg. **15**:438, 1928.

25. Miller, R., and Gage, H. C.: Gastromegaly and Chronic Duodenal Ileus in Children, Arch. Dis. Childhood **5**:83, 1930.

26. Weinbren, M., and McGregor, A. L.: Right-Sided Duodenum Inversum: A Record of Eleven Cases, Lancet **1**:280, 1934.

27. Jones, T. B., and Morton, J. J.: Congenital Malformations of the Intestine in Children, Am. J. Surg. **39**:382, 1938.

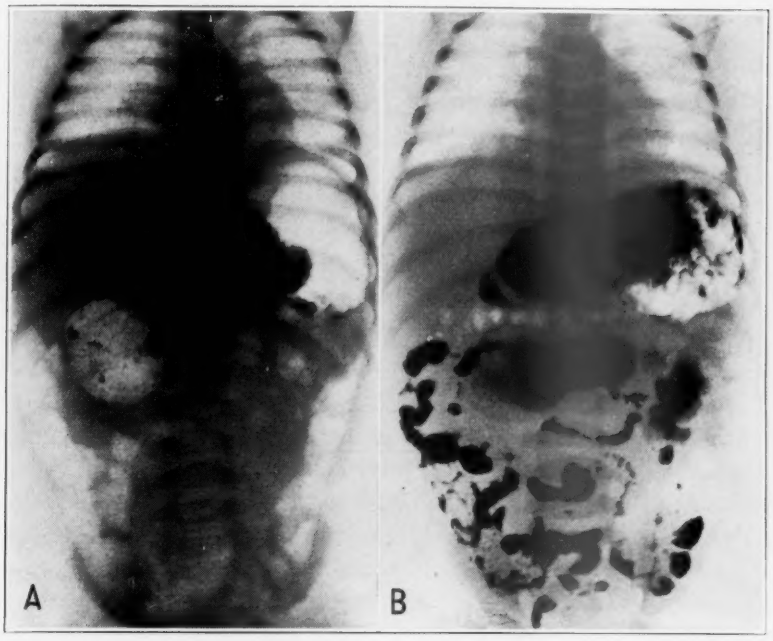

Fig. 7 (case 6).—Roentgenograms, taken with the patient in the prone position after an opaque meal: *A*, ten minutes after; *B*, an hour and a quarter after.

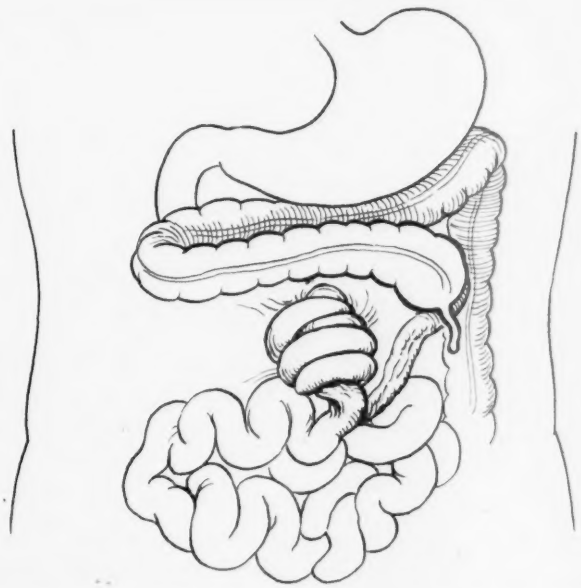

Fig. 8 (case 6).—Volvulus of the small intestine, with four turns about the axis of the mesenteric root.

cecum and the appendix lay in the left upper quadrant. The entire small intestine was twisted four full turns in a clockwise direction around the root of the mesentery, the lower half of the ileum being collapsed (fig. 8). The volvulus was reduced, and the cecum was attached to the lateral parietal peritoneum of the right lower quadrant.

Vomiting did not recur after operation, and the stools were normal as soon as an adequate caloric intake had been reached. The patient weighed 5,020 Gm. at the time of discharge, twenty-one days after operation. No information on the child's subsequent course is available.

The anatomic predisposition to volvulus of the part of the intestine arising from the midgut loop lies, as has been shown, in the narrowness of the root of its mesentery and in shortening of the duodenocolic isthmus. Such a volvulus may exist before birth, but this is evidently rare; the abnormality is usually produced by the motor activity of the digestive process. In all of the cases just described in which operation was done, symptoms set in within forty-eight hours of birth, and in 4 of them vomiting was described as beginning actually on the first day of life. On the other hand, the predisposition to volvulus may exist for a long time without the actual occurrence of volvulus itself. In case 6 there was a free interval of four months between the group of symptoms which occurred in the neonatal period and the syndrome dependent on the volvulus found at operation. The increasing frequency with which roentgenologists are discovering and reporting intestinal patterns compatible with comparable anomalies of development suggests too that among these cases of "mesenterium commune" (Altschul,[28] Janker,[21] Babaiantz and Kadrnka,[29] Spitz,[30] Belot and his co-workers,[17] Mazzini,[31] Cifone,[32] Gerscovich and Moreau,[33] Mandl,[34] Runco,[35] Martini and his

28. Altschul, W.: Mesenterium commune, Fortschr. a. d. Geb. d. Röntgenstrahlen **32**:580, 1924.

29. Babaiantz, L., and Kadrnka, S.: "Mésentère commun": Etude radiologique, J. de radiol. et d'électrol. **16**:251, 1932.

30. Spitz, L.: Ueber das Mesenterium commune und den Situs inversus partialis der Bauchorgane in der Röntgenliteratur: Drei weitere Fälle von Mesenterium commune, die klinische Bedeutung des Mesenterium commune, Fortschr. a. d. Geb. d. Röntgenstrahlen **46**:36, 1932.

31. Mazzini, O. F.: Duodeno anormal, sinistrocolia por colon movible, mesenterio común, Rev. de cir. de Buenos Aires **13**:40, 1934.

32. Cifone, A.: Sobre un caso de "mesenterium commune," Semana méd. **1**: 1150, 1935.

33. Gerscovich, J., and Moreau, M. H.: Mesenterium communis, Semana méd. **2**:1484, 1935.

34. Mandl, F.: Zur pathologischen Lage des Duodenum und der Flex. duodenojejunalis und ihre klinischen Folgeerscheinungen, Wien. med. Wchnschr. **85**: 289, 1935.

35. Runco, A.: Sul "Mesenterium commune," Radiol. med. **22**:147, 1935.

associates,[36] Bjelozerkowsky and Monblanow,[37] Charbonnier and Bardet[38] and Hormuth,[39] "cecum mobile" (Mazzini,[31] Desjacques[40] and Ibarz[41]), "nonrotation" (Rubin[42]), "duodenum inversum" (Weinbren and McGregor[26] and Mandl[34]) and "duodenum mobile" (Mandl[34]) there may be a considerable number of subjects who have a short duodenocolic isthmus and a narrow mesenteric root and yet have avoided a grade of torsion sufficient to induce ileus severe enough to demand operative intervention. The anatomic picture presented by some of the patients on whom autopsy was done who died without ever manifesting symptoms of significant alimentary obstruction (Ferrandu,[43] Gutiérrez,[44] Mazzini,[31] Pichler[45] and Rizzi[46]) does not differ discernibly from that of our patients in whom volvulus has been successfully reduced. These considerations lend probability to the belief that the symptoms of temporary duodenal obstruction sometimes observed in patients who present roentgen evidence of disturbances of intestinal rotation may reasonably be attributed to mild volvulus.

Two cases of this type are reported.

MALROTATION AND NONROTATION ASSOCIATED WITH SYMPTOMS OF TEMPORARY DUODENAL OBSTRUCTION NOT REQUIRING OPERATION

CASE 7.—Ernestine S. vomited sucrose solution on the day after birth, and on the second day the vomitus contained both fresh and old blood. Her weight, which had been 2,840 Gm. at birth, dropped to 2,420 Gm. on the third day, at which time transfusion, infusion and hypodermoclysis were administered, and the

36. Martini, T.; Dossola, A., and Noguera, O. F.: Acerca de una curiosa malformación de estómago: Dextrogastria asociada a un mesenterium commune, Semana méd. **1**:486, 1936.

37. Bjelozerkowsky, W., and Monblanow, W.: Mesenterium ileo-colicum commune, Zentralbl. f. Chir. **64**:208, 1937.

38. Charbonnier, A., and Bardet, P.: Un cas de "mésentère commun" chez une jeune femme, Rev. méd. de la Suisse Rom. **57**:863, 1937.

39. Hormuth, V.: Ein Fall von Mesenterium commune, Beitr. z. klin. Chir. **165**:641, 1937.

40. Desjacques, R.: Malformation congénitale du gros intestin (sinistrocolie au deuxième degré), Lyon chir. **33**:485, 1936.

41. Ibarz, P. L.: Observations de volvulus du caecum-côlon et de volvulus de l'ileo-caecum côlon ascendant, Lyon chir. **34**:370, 1937.

42. Rubin, E. L.: Radiological Aspects of Anomalies of Intestinal Rotation, Lancet **2**:1222, 1935.

43. Ferrandu, S.: Studio anatomico-patologico sul mesenterium commune nell'adulto e sulle distopie intestinali congenite, Ann. ital. di chir. **13**:511, 1934.

44. Gutiérrez, A.: Anomalía en la torsión del intestino medio, Rev. de cir. de Buenos Aires **13**:232, 1934.

45. Pichler, A.: Ueber einen Fall von Omentum duodenale bei Hemmung der Nabelschleifendrehung, Anat. Anz. **81**:159, 1935.

46. Rizzi, I.: Considerazioni anatomo-patologiche e cliniche sul mesenterium commune, Folia med. **23**:422, 1937.

gastrointestinal tract was examined roentgenographically. Barium sulfate passed the pylorus within a few seconds, encountering almost complete obstruction at approximately the junction of the first and the second portion of the duodenum. The duodenum above the obstruction showed moderate dilatation at times. At the end of one and a quarter hours only a small amount of the opaque meal was visible beyond the duodenum (fig. 9).

No gastric peristaltic waves were seen on physical examination, and a pyloric mass was not felt. The bleeding time and the coagulation time were normal on the third day. Even when given feedings of small volume the patient continued to vomit persistently for the first eight days of life, during which time the stools were infrequent and small. Repetition of the fluoroscopic examination at the age of 5 days disclosed an identical duodenal obstruction immediately after inges-

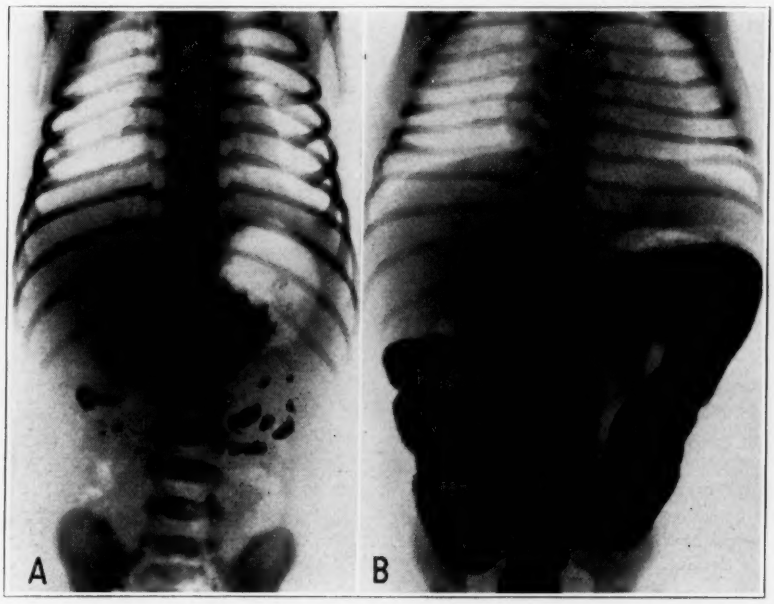

Fig. 9 (case 7).—*A*, roentgenogram taken an hour and a quarter after a barium sulfate meal was given, showing incomplete duodenal obstruction. *B*, roentgenogram taken after administration of a barium sulfate enema, showing the cecum high in the abdomen and close to the midline.

tion of the opaque meal, though under continued observation it was evident that the severity of the block had decreased. At the age of 9 days the colon was satisfactorily filled with a suspension of barium sulfate by holding the patient inverted during the injection, and the organ was found to be of normal caliber; the cecum lay approximately in the midline, high in the abdominal cavity; no ascending colon could be made out, and the transverse colon was doubled on itself. The association of malrotation of the portion of the intestine originating in the midgut loop with duodenal obstruction thus suggested strongly the possibility of volvulus.

Vomiting ceased on the eighth day; the stools increased in volume and number, and the patient commenced to gain, reaching her birth weight on the thirteenth

day. From this time on she made satisfactory progress. Barium sulfate enemas repeated at the ages of 10 and 11½ months showed the cecum lying in the right half of the abdomen but with its tip rather high. At the time of writing the patient is being kept under close observation.

The absence of bile in the vomitus, in the presence of roentgenographically proved duodenal obstruction, is not readily explained. The obstruction, which was localized at the junction of the first and the second portion of the duodenum, may have been above the ampulla of Vater, though this is rare in the type of disturbance associated with errors of rotation. Hematemesis in this case may have been an expression of hemorrhagic disease of the newborn, especially since it occurred only on the second day of life and was not observed after transfusion. Dott [2] mentioned hematemesis in cases of volvulus of the section of bowel arising from the midgut loop, but it is likely to be found in the patients who die rather than in those who survive.

CASE 8.—Junius C. vomited bile-stained material on the sixth day of life, and his neonatal loss of weight persisted. Physical examination showed nothing abnormal. On fluoroscopic study the stomach was seen to be of average size, and the duodenum could not be clearly outlined; the jejunum lay on the right side of the spine, and there was 50 per cent retention of gastric contents after six and three-quarters hours (fig. 10). Vomiting ceased by about the tenth day of life, and the number of stools increased to six a day. From then on the rate of gain was rapid, the patient reaching a weight of 4,635 Gm. at the age of 6 weeks and 9,770 Gm. at 6½ months. Repetition of roentgen examination at 6 months showed the jejunum to lie entirely in the right half of the abdominal cavity; the cecum was in the left upper quadrant. The patient still tends to regurgitate but has not vomited bile since the neonatal episode. He is being followed in the outpatient clinic.

In this group of cases taken as a whole there were 6 patients with proved volvulus of the portion of the intestine derived from the midgut loop and 2 with postulated volvulus. One patient had two attacks of volvulus which were identified surgically and subsequent attacks of comparable symptoms, which justified an inference of additional recurrences. Another patient recovered spontaneously from an attack of duodenal obstruction in the neonatal period, with recurrence of symptoms and proved volvulus at operation at the age of 5 months. All of the patients in the group exhibited signs of duodenal obstruction within the first week of life, and all but 1, within the first two days. Five of them came to operation within the first two weeks of life. There was 1 death in the series. Three of the patients were boys and 5 were girls.

The clinical picture of volvulus associated with errors of rotation of the midgut has been frequently described. (A summary of the literature up to 1934, with tabulation of the reported cases, was given by Gardner

and Hart.[5] Since then, descriptions of cases in which symptoms of volvulus developed immediately after birth have been published by Bauer,[47] Berman,[48] Edwards,[49] Reisman,[50] Sturrock [51] and Cathcart; [52] with symptoms developing within a few days after birth by Siddiqi,[53] Hipsley,[54] Turunen,[55] Borow [56] and Rosenblatt,[12] and with proof of volvulus brought out at a later age by Heise,[57] Liebe,[20] Dixon and Deuterman,[23] Donaldson,[58] King,[18] Koszler [19] and Clausen,[8] among others.) As Gardner and Hart [5] emphasized, the effect of volvulus under these circumstances is at first to produce partial obstruction of the intestinal lumen at the duodenojejunal junction without shutting off the blood supply, so that the syndrome of mechanical ileus, uncomplicated by that of gangrene of the intestines, dominates the clinical picture. In time the obstruction may be complete; but this is surprisingly rare, occurring in only 1 case in our series. At the same time, the obstruction to passage of intestinal contents is sufficiently complete and occurs at a high enough level to cause bilious vomiting as the outstanding symptom. It was lacking in one of our cases, in which the assertion of duodenal obstruction rested largely on roentgen evidence. Vomiting is usually, though not always, projectile. Appetite is for the most part not seriously impaired, initially at least, but the failure to retain food accentuates and prolongs the neonatal loss of weight. In several instances a change of feeding was tried without benefit. The stools are

47. Bauer, G.: Störung der Entwicklungsmechanik der Darmdrehung unter Einfluss einer Darmstenose, Centralbl. f. allg. Path. u. path. Anat. **63**:193, 1935.

48. Berman, J. K.: Congenital Anomalies of the Midgut, Internat. Clin. **4**: 240, 1937.

49. Edwards, H.: Exomphalos Associated with Volvulus Neonatorum: Result Six and a Half Years After Operation, Proc. Roy. Soc. Med. **30**:881, 1937.

50. Reisman, H. A.: Congenital Obstruction of the Alimentary Tract, J. Pediat. **10**:622, 1937.

51. Sturrock, J.: Volvulus of the Whole Small Intestine, Tr. Edinburgh Obst. Soc., 1934-1935, p. 62; in Edinburgh M. J., May 1935.

52. Cathcart, D. F.: Congenital Intestinal Anomaly in a Newborn Infant, Am. J. Dis. Child. **55**:566 (March) 1938.

53. Siddiqi, M. A. H.: Volvulus in a Newborn Child, Indian M. Gaz. **69**: 264, 1934.

54. Hipsley, P. L.: A Case of Malrotation of Midgut Loop with Superimposed Volvulus, M. J. Australia **1**:716, 1935.

55. Turunen, A. O. I.: Einige Fälle von Darmverschluss bei Neugeborenen, Acta Soc. med. fenn. duodecim (Ser. B, fasc. 1-3, art. 14) **23**:1, 1935.

56. Borow, B., and Borow, H.: Operation for Volvulus with Recovery, J. A. M. A. **108**:43 (Jan. 2) 1937.

57. Heise, W.: Volvulus des gesamten Dünndarms und des Colon ascendens, Zentralbl. f. Chir. **62**:382, 1935.

58. Donaldson, H. H.: Abnormalities of Rotation of Midgut, Am. J. Surg. **32**:352, 1936.

diminished in quantity, though often remaining normal in number. The histories contain several descriptions of "starvation stools"; these were green, and of small volume, consisting mainly of bile-stained mucus; they supervened on the evacuation of normal meconium. Constipation was noted at times. The young patients fail to present clear evidence of associated pain. As a result of persistent vomiting, there is a significant drain on the body stores of water and electrolytes, especially sodium chloride.

Because the obstruction gives rise to demonstrable gastric and often also duodenal dilatation and because the alimentary tract below the level of obstruction is usually more or less collapsed at operation, stress has

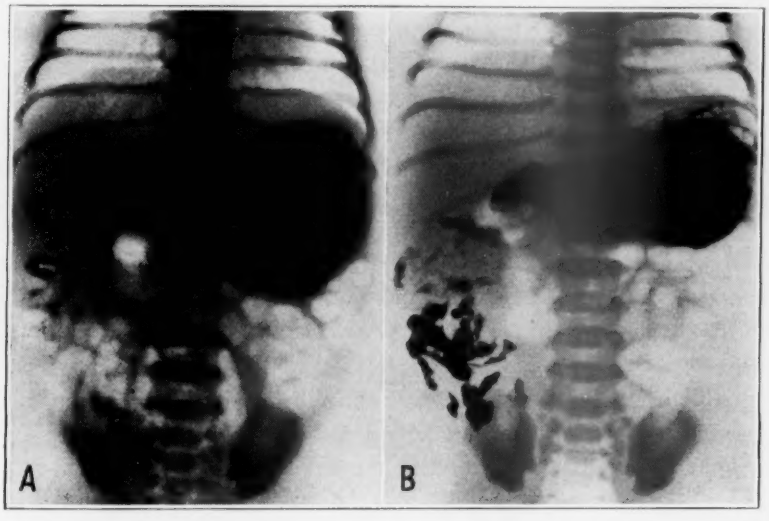

Fig. 10 (case 8).—Roentgenogram, taken after an opaque meal: *A*, one hour after; *B*, two hours after. There is partial obstruction of the duodenum, with distortion of its channel. Note the small caliber of the jejunal coils, which lie to the right of the spine.

been laid in some of the published descriptions (Clausen;[8] Dott;[59] Morton and Jones[60]) on the clinical finding of epigastric distention with collapse of the abdomen below it. We have not observed this in any of our cases of volvulus of the portion of intestine originating in the midgut loop. The explanation may be that with only partial obstruction the bowel is at least partly distended, and because it is bunched together in the tangled mass hanging from the mesenteric root it occupies enough volume to fill out the abdominal contour. In our series generalized abdominal distention was found only once; gastric distention was of

59. Dott, N. M.: Volvulus Neonatorum, Brit. M. J. **1**:230, 1927; footnote 2.

60. Morton, J. J., and Jones, T. B.: Obstructions About the Mesentery in Infants, Ann. Surg. **104**:864, 1936.

varying incidence, for some patients appeared to empty their stomachs on the slightest provocation of overfilling, while in others the threshold of emesis seemed to be higher. Gastric peristaltic waves were observed in less than half of our cases; a pyloric mass was palpated in 2.

MALROTATION WITH PATHOLOGIC FIXATION OF THE DUODENUM

Another group of patients showed obstruction from fixation of the duodenum in an abnormal position, sometimes with kinking or compression of the lumen by peritoneal bands or adhesions. The regularity with which bands and adhesions occur in conjunction with anomalies of intestinal rotation has been emphasized by virtually all students of this problem, whether they have approached it from the purely anatomic point of view or from the clinical side as well, and our observations coincide with theirs. The incidental nature of such bands was fully established long ago by Frazer and Robbins,[1] who proved conclusively that they were the result, rather than the cause, of anomalies of rotation. These authors showed, moreover, that certain constant and well established areas of thickening in the parietes of the peritoneal cavity are the normal residua of the process of intestinal rotation; but in spite of their clear exposition and indubitable proof of the nature of these structures, a tendency still persists for surgeons and pathologists as well to regard them as "adhesions" of inflammatory origin, traceable to antenatal "peritonitis."

Bands of this sort are easily recognized at operation, if proper care is taken to visualize the duodenum throughout its course, whereas anomalies of the disposition of the intestines are much less obvious and have been known to escape full appreciation on the part even of experienced surgeons. The literature of the subject contains a number of reports of this kind of case, in which symptoms were wrongly ascribed to the existence of a congenital peritoneal band when in reality the primary fault was one of rotation. We have come to believe that obstruction by peritoneal bands rarely occurs when the rotational process has progressed normally; certainly in our own experience this occurrence is rare.

CASE 9.—Joan W. began vomiting on the day after birth, and the vomitus soon became bile stained. At the time of admission to the hospital, at the age of 7 days, she was said to have passed no stools. At this time she weighed 2,430 Gm., was dehydrated and had a temperature of 103 F. Gastric peristaltic waves were observed. When a wave progressed to the pylorus, one could feel fluid squirting under the finger in the right upper quadrant. The pylorus was palpable, as was a softer mass beyond it which was thought to be distended, tense duodenum. Gastric lavage yielded bile-stained fluid. Fluoroscopic study showed prompt passage of opaque material out of the stomach, but there was marked delay in emptying of the first portion of the duodenum, which was

dilated. There was practically no barium sulfate in the jejunum seven hours after administration of the meal, and but little was noted seventeen hours after. An obvious and almost complete duodenal obstruction existed at about the level of the duodenojejunal junction.

Operation was performed on the day after the patient's admission, when she was 8 days of age. When the abdominal cavity was opened, the small intestine presented. In tracing it both distally and proximally the operator always came to the cecum; on removal of the entire small intestine from the abdominal cavity, this peculiarity was accounted for by the fact that the proximal end of the jejunum was bound to the distal end of the ileum by an adhesion (fig. 11) and, in addition, by volvulus of the part of the bowel arising from the midgut loop, which was twisted one and a half turns in a clockwise direction about its narrow mesenteric pedicle. The duodenum was sharply kinked on itself at

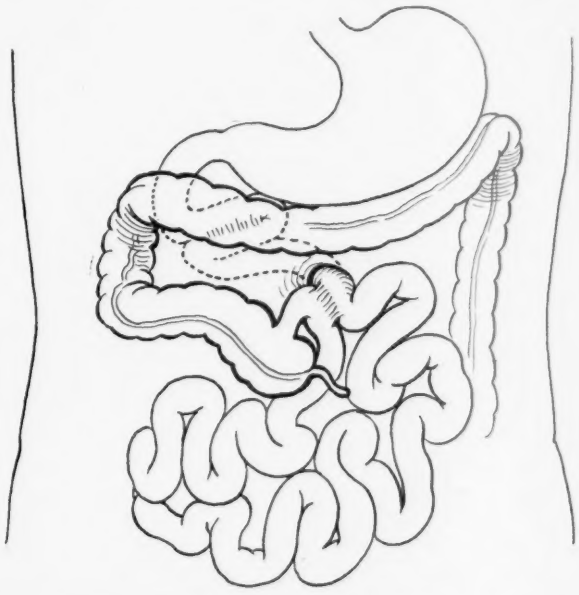

Fig. 11 (case 9).—Diagram showing the distortion of the duodenum and the adhesions binding the lower part of the ileum and the upper part of the jejunum. The volvulus has been reduced.

about the junction of the second and the third portion, so that the third portion coursed from left to right in place of continuing the normal C curve; firm bands maintained the kink. The ileocecal junction lay in the upper part of the abdomen in the midline. The volvulus was untwisted, and the duodenal and ileojejunal bands were divided.

Bleeding from the wound required transfusion the day after operation. The wound then became infected; vomiting persisted, and there was marked diarrhea. On the seventh postoperative day, during the process of dressing, the wound broke wide open and allowed the intestines to protrude. The patient was taken to the operating room, and the wound was sewed up. Transfusion was administered three times more. The infection of the wound gradually subsided. At the time of the patient's discharge, twenty-seven days after operation, she weighed

3,080 Gm. A cephalematoma, which had been present during her stay in the hospital, became infected and required incision and drainage a few days after her return home. In spite of this complication, the child made a satisfactory convalescence, remained free from digestive symptoms and at the age of 6½ months weighed 7,950 Gm. At 2½ years she weighed 12.73 Kg. and was in excellent health, being free from digestive symptoms.

In this case of nonrotation of the bowel, volvulus of the entire small intestine was found together with fixation of the duodenum by peritoneal bands; it was the operator's impression that the latter lesion was the more important in causing duodenal obstruction. Ladd [61] stressed the necessity of thoroughly investigating the duodenum in every case of malrotation in which operation is performed, whether volvulus is present or not, and of freeing it as far as possible from extrinsic causes of block. Such bands when divided show no particular tendency to recur. The palpability of the pylorus in this case is noteworthy, as is also the full recovery after postoperative eventration.

CASE 10.—John K. vomited bile-stained material on the first day of life and continued to do so up to the time of admission to the hospital, at the age of 15 days. Breast feeding was discontinued on the second day, and various formulas were tried without relief from symptoms. The appetite remained good, and the stools were said to be normal. On admission the infant weighed 2,250 Gm. and was feeble, malnourished and dehydrated. The abdomen was scaphoid; no peristaltic waves were seen, and the pylorus was not palpable. Projectile vomiting of bile-stained material was observed. On fluoroscopic examination the stomach was seen to be distended (fig. 12). After one-half hour the barium sulfate meal had passed the pylorus but had not gone beyond the first few centimeters of the duodenum, which was not greatly increased in caliber. After three hours a few flakes of barium sulfate had entered the small intestine.

Operation was performed when the patient was 16 days of age. The cecum and appendix were found in the left upper quadrant. The normal fusion between the gastrocolic ligament and the transverse mesocolon was lacking. The duodenum passed directly downward through the transverse mesocolon on the right side of the vertebral column, so that the fossa of Treitz was on the right (fig. 13). Adhesions between the ascending and the transverse colon held the former in an abnormal position. The entire small intestine beyond the first 10 cm. of the jejunum was turned once counterclockwise around the mesenteric root, the bowel being collapsed beyond the obstruction. After section of the adhesions the volvulus was untwisted, and the organs were returned to their normal positions without fixation by suture.

Although vomiting ceased after operation, the patient failed to thrive in spite of repeated transfusions and other supportive measures. The abdominal wound became infected and broke open, requiring resuture seven days after operation, and the transfusion wounds at both ankles likewise became infected. The course was gradually downward, the patient dying at the age of 33 days. The blood was not cultured during life. Autopsy showed icterus, infection and disruption of the laparotomy wound, fibrous peritoneal adhesions, malrotation of the

61. Ladd, W. E.: Surgical Diseases of the Alimentary Tract in Infants, New England J. Med. **215**:705, 1936; footnote 11.

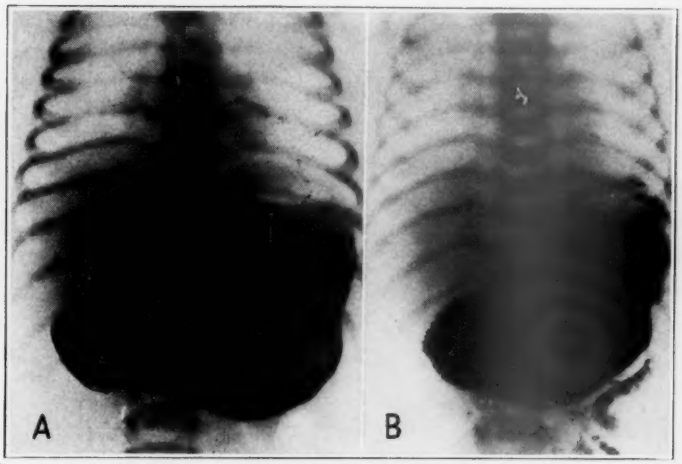

Fig. 12 (case 10).—Roentgenograms taken after an opaque meal: *A*, one-half hour after; *B*, twenty-four hours after. There is dilatation of the stomach and duodenum, with almost complete duodenal obstruction.

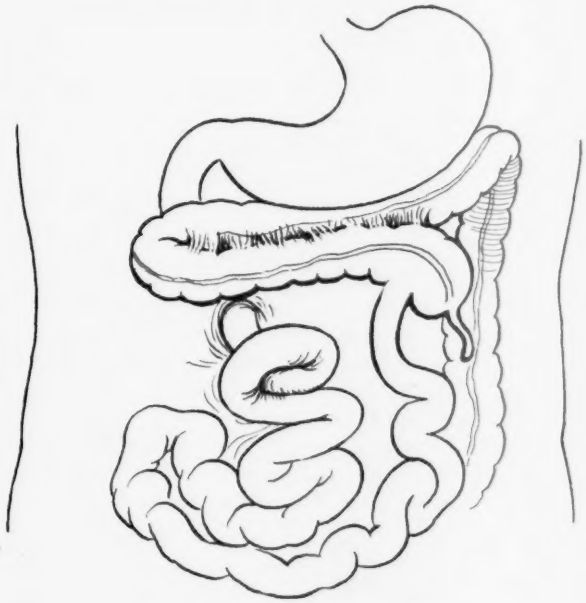

Fig. 13 (case 10).—Abnormal fixation of the duodenojejunal junction, the fossa of Treitz lying to the right of the vertebral column; there are adhesions between the ascending and the transverse colon. The volvulus has been reduced.

intestines, thrombosis of a pulmonary vein, abscesses in the heart, lungs, spleen, liver, kidneys and skin and hemorrhages in the lungs. Postmortem blood culture yielded a hemolytic strain of Staphylococcus aureus.

In this patient the degree of disturbance of the rotational process amounted almost to nonrotation. As in case 9, both volvulus of the entire small intestine and hyperfixation of the duodenum were present, and here too it was the operator's impression that the latter lesion was the more important in causing obstruction. Cathcart [52] reported a case of a somewhat similar condition. After successful surgical reduction of volvulus at the age of 2 days, a return of symptoms at 1½ months demanded a second exploration. At this time was found constriction of the duodenojejunum as it passed through the mesentery of the small intestine in the right lower quadrant; after duodenojejunostomy the patient recovered.

CASE 11.—Patrick A. began vomiting on the day after birth. Little information was given by the parents, so that it was not known when bile first appeared in the vomitus. Weaning and various changes of formula failed to dispel the patient's symptoms, and he was seen in consultation at the age of 11 days by Dr. F. H. Bartlett, who observed bilious vomiting and referred him to the hospital. His weight at the age of 12 days, 3,100 Gm., was 625 Gm. less than his birth weight. Gastric peristaltic waves were visible in a distended stomach, and in the right upper quadrant a dilated loop of intestine could be felt. Normal stools were passed. Fluoroscopic study showed a slightly dilated stomach with a patent pylorus; the duodenum, which was moderately distended and fluctuated considerably in size in periods of contraction and relaxation, presented a partial obstruction to passage of the meal at the duodenojejunal junction, below which the intestine had a conspicuously narrow lumen (fig. 14). Under conservative treatment the patient failed to improve, and operation was performed at the age of 20 days.

The duodenum, leaving the stomach normally, coursed downward and to the right, lying behind and laterally to the proximal part of the colon, to emerge in the right lower quadrant at the usual position of the ileocecal valve (fig. 15). Its attachment to the posterior abdominal wall was at first above and later lateral to that of the adjacent colon. At its point of emergence, its channel formed an acute angle maintained by peritoneal bands, the obvious site of obstruction. Section of some of these bands allowed the duodenojejunal junction to straighten somewhat. Nothing further could be done surgically to restore normal relationships.

On gradual increase of caloric intake in the postoperative period the patient remained free from vomiting. He has remained well, and at the age of 15 months weighed 12.73 Kg. and had no digestive symptoms.

The anatomic picture in this case differed from that of simple nonrotation in the unusual fixation of the duodenum and in the more nearly normal pattern of the large bowel. It could have been caused by return of the postarterial segment of the midgut first into the abdomen from the umbilical cord, the segment then attaching itself to the posterior abdominal wall before the duodenum could take up its normal position.

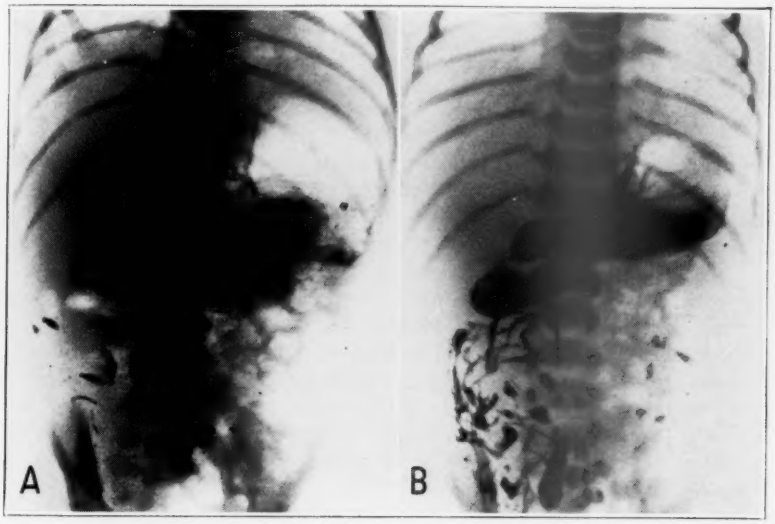

Fig. 14 (case 11).—Roentgenograms taken after an opaque meal: *A*, two hours after; *B*, four hours after. There is partial obstruction of the duodenum, with distortion and dilatation of its channel. In *B*, note the position of the jejunum on the right and the small caliber of its coils; the mass lying against the lower part of the spine represents cecum, while the central mass of barium sulfate just below the stomach probably represents a portion of the transverse colon.

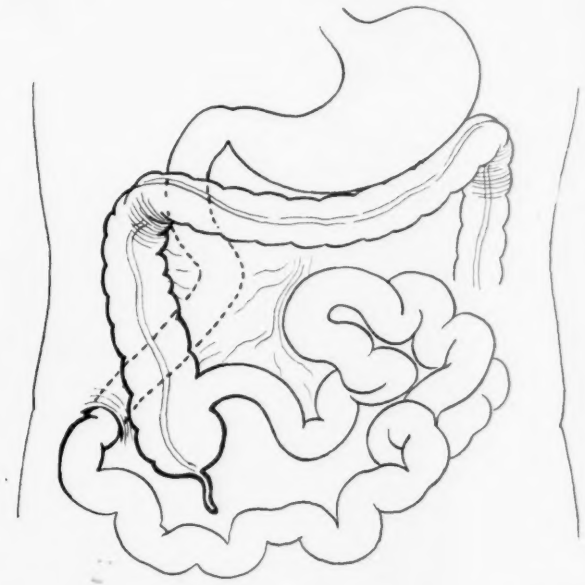

Fig. 15 (case 11).—Sketch of the abnormal course of the duodenum and the proximal part of the jejunum.

This condition differs from reversed rotation by the circumstance that in the latter the duodenum passes downward in front of the transverse colon. No true twisting of the bowel about its mesentery was found.

CASE 12.—Joyce W. had bilious vomiting on the second day of life. The stools were small and greenish brown. At the age of 6 days fluoroscopic study showed an obstruction at what seemed to be the duodenojejunal junction, with a 70 per cent residue proximal to this point after two and one-half hours. Three days later, when the patient was 9 days old, examination suggested relaxation of the obstruction; but bilious vomiting persisted, and the patient failed to gain. She was admitted to the hospital at the age of 12 days. Physical examination gave essentially normal results. In spite of two days of starvation and subsequent gradual increase in the caloric intake, bilious vomiting continued, and the stools failed to attain a normal appearance. A third roentgen examination, carried out at the age of 24 days, showed duodenal dilatation with partial obstruction at the duodenojejunal junction, the degree of block now being more severe than ever. The cecum lay high in the right side of the abdomen. Preoperative diagnosis of volvulus of the portion of bowel derived from the midgut loop was made.

The patient was operated on at the age of 29 days, her weight at the time being 2,560 Gm. Volvulus, with one and a half clockwise turns, was discovered; it involved the lower end of the mesenteric root and the terminal part of the ileum. The twist seemed loose, which suggested an additional obstruction at a higher level. The stomach was normal; the duodenum was moderately dilated and passed normally below the hepatic end of the transverse mesocolon. However, instead of then swinging back to the left to the location of the duodenojejunal ligament, the duodenum continued straight down, parallel to the cecum, and the upper part of the jejunum passed directly through the mesentery of the intestine close to the mesenteric attachment of the terminal part of the ileum (fig. 16), thus hobbling the whole small intestine in a loop shaped like a horseshoe. The mobile cecum was in normal position, the appendix lying retrocecally. The volvulus was unwound, and the cecum was anchored to the lateral peritoneal wall with three catgut sutures.

A small amount of vomiting persisted for two days after operation, then ceased except for occasional regurgitation of bile-free gastric contents, which was considered to be within normal limits. Diarrhea, brought on by infection of the respiratory tract, began on the seventh postoperative day and continued for two weeks, though gain in weight was not interrupted. On discharge, at the age of 2 months, the patient weighed 3,350 Gm. At 5 months she weighed 5,680 Gm. and was free from digestive symptoms.

Again in this case volvulus of part of the portion of bowel originating in the midgut accompanied an abnormal course of the distal portion of the duodenum, but here it was the volvulus that appeared to be the dominant cause of obstruction. The upper end of the jejunum passed through a tunnel in the mesentery of the terminal part of the ileum and reappeared below it, and it was the bight of bowel between this point and the terminal part of the ileum that was twisted on its mesenteric attachment. If in the return of the midgut from the umbilical cord in the second stage of rotation the upper part of the jejunum happened to

get anchored to the posterior abdominal wall by adhesions which fixed its position to the right of the spinal column and caused it to course straight downward from the second portion of the duodenum, then the formation of this apparent tunnel through the mesentery of a more caudal portion of the midgut (in this case, the terminal portion of the ileum) would follow automatically whenever the fixation of the mesentery to the posterior abdominal wall progressed downward and to the right far enough to jump over the upper segment of jejunum which was attached in the unusual manner described. The mesenteric root had the narrowness of base which predisposes to volvulus, since the duodeno-

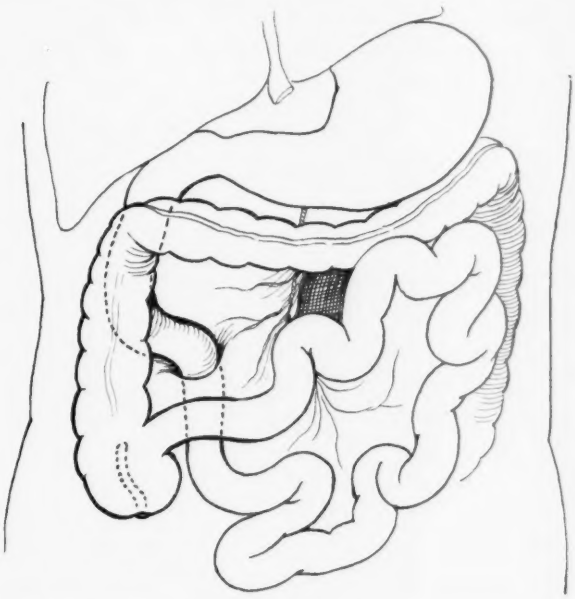

Fig. 16 (case 12).—Diagram of the anomaly after reduction of the volvulus. The jejunum, after leaving the duodenum, emerges from a tunnel in the mesentery of the terminal part of the ileum.

jejunal junction was abnormally placed downward and to the right and thus closely approached the attachment of the mesentery of the terminal part of the ileum. Although surgical restoration of normal relationships of the bowel and its attachments was not feasible in this case, it is hoped that fixation of the cecum will prevent a recurrence of volvulus.

CASE 13.—Elsie R. began to have projectile vomiting at the age of 2 weeks; it continued for ten weeks, up to the time of admission to the hospital, when she was 3 months old. At first the vomitus was greenish; later it was described as fecal. The patient was nursed up to three days before admission. During the four weeks preceding admission she was under observation in another hos-

pital, where she showed some improvement in the severity of vomiting on a regimen of underfeeding and lavages, though her loss of weight progressed. Her appetite remained unimpaired. On examination she was emaciated and dehydrated and weighed 2,800 Gm. The abdomen was distended and tense, and gastric peristaltic waves were seen, but no pyloric mass was felt. One observer described a mass suggestive of dilated duodenum. Bilateral purulent otitis media was present.

After transfusion, parenteral administration of a solution of sodium chloride and other supportive measures, operation was performed. The stomach and the first portion of the duodenum were enormously distended. In the second portion of the duodenum the intestine was sharply flexed on itself, the distal part below the kink being of subnormal caliber and coursing to the right. The cecum lay close to the midline, and the appendix, attached by a long mesentery, was situated under the liver. The duodenum was freed to some extent by section of the bands which bound it to the posterior abdominal wall and maintained the angulation.

The patient died a few hours after operation. Autopsy showed thickening of the wall of the stomach in its antral portion. The dilated first part of the duodenum measured 4.5 cm. in length and 4 cm. in diameter. The kink found at operation in the second portion of the duodenum was again observed. Peritoneal bands ran from the region of the gallbladder to the duodenum. Most of the jejunum was situated in the right half of the abdominal cavity, and the ileum entered the nonrotated cecum from the right.

The fatal outcome in this case emphasizes the added surgical risk when the effort to control symptoms by conservative measures is unduly prolonged. A 3 month old infant weighing 2,800 Gm. is less likely to withstand the operative procedure than a much younger infant of the same size. Full cooperation between surgeon and pediatrician is essential in these difficult situations, and each must have due appreciation of the part which the other is equipped to play in the therapeutic program.

In this group of 5 cases of errors of intestinal rotation with accompanying obstruction of the duodenum by persistent peritoneal bands, it will be noted that there were 3 instances (cases 9, 10 and 12) in which volvulus of a large segment of the part of the intestine derived from the midgut was also present. When both of these modes of obstruction coincide, it is largely a matter of opinion which of them is of the greater clinical significance in a given case; but the question is of secondary importance, since the necessity for correcting both of them is only too obvious. The therapeutic point to be emphasized is the importance, in every case of volvulus dependent on an anomaly of rotation, of visualizing the duodenum so that the double lesion, if present, may be identified and corrected.

Cautley [62] reviewed the subject of congenital duodenal fixation in 1919, and Gardner and Hart [5] summarized the literature up to 1934. More recently, cases in which operation was done during infancy have

62. Cautley, E.: Duodenal Stenosis, Brit. J. Child. Dis. **16**:65, 1919.

been described by Hipsley,[63] Dobbs and Heritage,[64] Morton and Jones,[60] Berman [48] and Clausen; [8] during childhood, by Koszler; [19] in adult life, by Wakefield and Mayo [6] and Bjelozerkowsky and Monblanow.[37] It is evident that the proportion of operative recoveries is increasing. Earlier diagnosis and improvement in preoperative preparation as well as in postoperative care combine with advances in surgical technic to bring about this result.

VOLVULUS OF THE PORTION OF INTESTINE DERIVED FROM THE MIDGUT ASSOCIATED WITH ATRESIA OF THE ILEUM

In the following case there were multiple causes of obstruction. The patient did not survive. The cases of Hipsley [54] and Bauer [47] are comparable in the exhibition of coexisting varieties of developmental obstruction, one of which was volvulus of the part of the intestine derived from the midgut loop.

CASE 14.—Ruth K. began vomiting bile-stained material thirty-two hours after delivery and continued to vomit forcibly during almost every feeding. After the evacuation of meconium, the appearance of the stools suggested that some food was passing the obstruction. Roentgen examination made prior to the child's admission to the hospital showed gastric retention with partial duodenal obstruction. When the patient was admitted, at the age of 2 days, she was apathetic, dehydrated and jaundiced. The vomitus was brilliant green. The abdomen was distended, and there was dilatation of the superficial veins over the lower part of the thorax and the anterior abdominal wall. No peristaltic waves were seen, and no pyloric mass was felt. Fluoroscopic study showed some barium sulfate remaining in the dilated stomach; loops of small intestine occupied all of the abdominal cavity except the right lower quadrant, but there was no barium sulfate caudal to the stomach.

When the patient was 2 days old, after transfusion and infusion, an exploratory operation was done. The peritoneal cavity contained about 50 cc. of clear bile-stained fluid. The presenting coils of small intestine showed purplish discoloration and were twisted into a mass which, on separation, revealed volvulus of the midportion of the ileum, in the center of which there was atresia of the intestine (fig. 17). Below this the intestine was collapsed, and above it, dilated. Between these two areas there was a small whitish narrowed portion about 1.5 cm. in length and 5 mm. in diameter. All loops of bowel were somewhat adherent and were covered with fine fibrinous exudate. Just beneath the atretic portion of the ileum there was a large defect in the mesentery about 5 by 8 mm. in diameter; none of the intestine was herniated through it. The entire midportion of the ileum, including the volvulus, was matted together into a mass about the size of a hen's egg, which was adherent in the right lower quadrant just below and somewhat medially to the cecum. The volvulus was unwound, the atretic portion of ileum was resected, a side to side anastomosis was per-

63. Hipsley, P. L.: Deficient Fixation with Probable Volvulus of the Midgut Loop in an Infant, M. J. Australia **1**:463, 1935.

64. Dobbs, R. H., and Heritage, K.: Malrotation of the Intestines in a Child Aged Nine Months; Cured by Operation, Proc. Roy. Soc. Med. **30**:404, 1937.

formed, and the defect in the mesentery was repaired. After completion of the anastomosis the loops of matted bowel still had purplish discoloration but were apparently viable.

The patient died about twenty hours after operation. Autopsy showed hemorrhages into the mesocolon and the peritoneal cavity. The duodenocolic isthmus was narrow. The portion of intestine involved in the volvulus was histologically viable, in spite of thinning of the wall and sloughing of the mucosa. The stoma of the anastomosis was patent, and its walls were tight. No histologic evidence of infection was found in the peritoneal cavity, although cultures revealed a few organisms, chiefly Streptococcus viridans. There were pulmonary edema and lobular pneumonia, together with evidence of aspiration of amniotic fluid.

In the following case a disturbance of intestinal rotation was evident, but the exact cause of duodenal obstruction was not discovered. Possibly there was associated intrinsic obstruction from failure of reestablishment of the lumen of the bowel during the early weeks of intrauterine life.

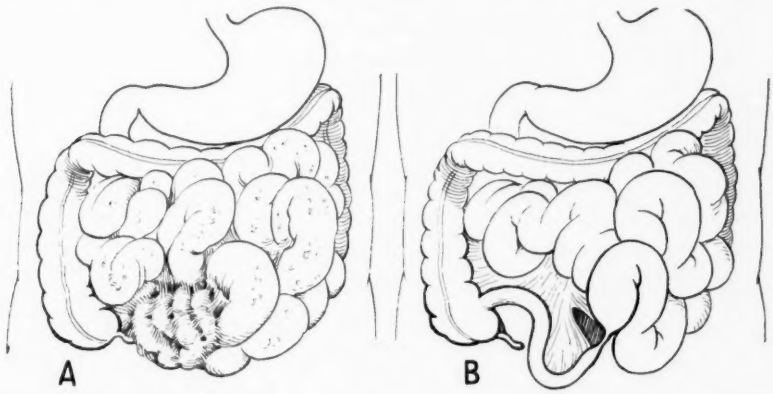

Fig. 17 (case 14).—Diagram of the anomaly: *A*, appearance when the peritoneal cavity was opened; B, after partial reduction of the volvulus. There is a defect in the mesentery of the ileum adjacent to the site of atresia.

CASE 15.—In Baby W. vomiting developed on the first day and increased in severity; the material expelled was at first bile stained and later chocolate colored. Weaning failed to cause improvement. Meconium and mucus were passed, but no fecal stools. On admission to the hospital, at the age of 4 days, the boy was feeble, with dehydration and obviously marked loss of weight. The abdomen was not distended. Roentgen study with an opaque meal showed complete duodenal obstruction at about the junction of the first and the second portion.

At operation, performed at the age of 4 days, the stomach and the first and middle portions of the duodenum were greatly dilated. When the transverse colon was lifted, it was found that there had been incomplete rotation of the intestine; the ascending colon was parallel with the transverse colon, and the termination of the small intestine was adjacent to the upper part of the jejunum (fig. 18). This condition was verified after the entire small intestine had been followed, from the cecum to the point at which the jejunum emerged from behind the transverse mesocolon. The cause of dilatation of the duodenum was not demonstrated. Duodenojejunostomy was performed.

Vomiting of bile-stained material persisted in spite of gastric lavage and underfeeding, and the patient died six days after operation. Permission for further examination was withheld.

NONROTATION WITH MOVABLE CECUM ASSOCIATED WITH ATTACKS OF NAUSEA AND VOMITING

CASE 16.—Since the age of 2 years Anne P. had suffered from attacks of nausea and vomiting which recurred every twelve to sixteen months and lasted from two to five days. When she was 9 years old roentgen examination by Dr. C. G. Kerley revealed nonrotation of the intestine, and she was referred for operative correction to Dr. J. M. Hanford, who permitted us to include this case in our series. She weighed 23.35 Kg. The abdomen was scaphoid, and no

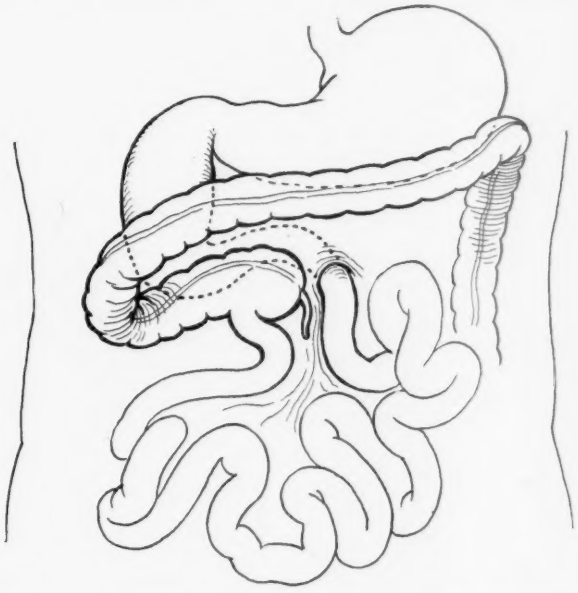

Fig. 18 (case 15).—Incomplete rotation of the part of the intestine originating in the midgut loop, with a narrow mesenteric root but without volvulus. The cause of duodenal obstruction may have resided in an associated intrinsic lesion.

masses were felt. Confirmatory examination after a barium sulfate enema on the patient's admission to the hospital showed displacement of the entire proximal part of the colon into the left half of the abdomen, the cecum being high and movable and the ileum entering it from the right.

At operation the common mesentery of the small intestine and the proximal part of the colon were found to be unusually long. There was failure of rotation of the section of intestine arising from the midgut loop, the jejunum lying in the right side of the abdomen (fig. 19). The appendix, which was long and somewhat congested, was removed. The proximal portion of the transverse colon was brought over to its normal bed beneath the liver and sutured to the lateral parietal peritoneum, and a comparable procedure of fixation was applied to the ascending colon and the cecum.

Immediately after operation the patient suffered from considerable vomiting, which continued for about three days, with dehydration and ketosis; but she responded to parenteral administration of fluids. On the fifth postoperative day dysuria and gross hematuria developed, both of which disappeared within twenty-four hours. Thereafter convalescence was uneventful, and the patient has remained free from digestive symptoms during the year that has elapsed since operation.

The unspecific nature of this patient's attacks and the long intervals between them throw doubt on their relation to the developmental anomaly encountered, and the period of observation after surgical fixation of the proximal portion of the large bowel is still too short, at the time of writing, to admit of final evaluation of the efficacy of this procedure. It was the operator's impression that the symptoms of which the patient complained had been caused by the unusual mobility of this

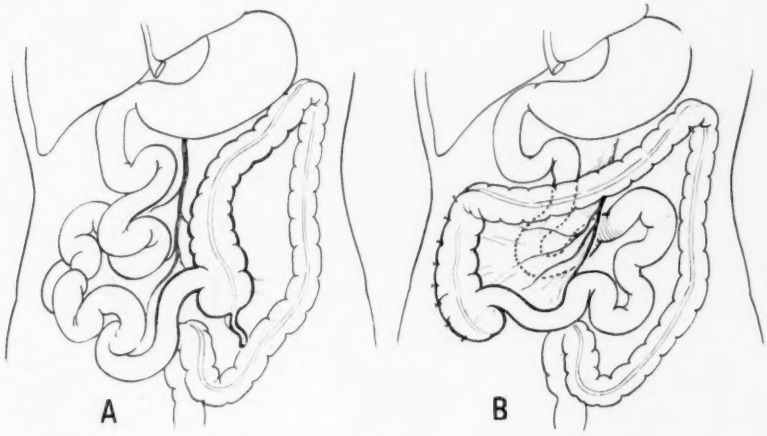

Fig. 19 (case 16).—Diagram of the anomaly: *A*, nonrotation, as found at operation; *B*, appearance after surgical fixation of the proximal portion of the colon and the cecum.

part of the intestine. In time the significance of their association may become clear. Danelius [65] described patients who had comparable symptoms and roentgen evidence of underlying errors of intestinal rotation, but in no case was there surgical verification of the diagnosis or correction of the condition.

MALROTATION WITH VOLVULUS ASSOCIATED WITH SITUS INVERSUS ABDOMINALIS PARTIALIS

CASE 17.—Richard D. first had mild vomiting at the age of 9 days, when he was taking bottle feedings. Gradually this became more severe, and at the age

65. Danelius, G.: Abnormalities of the Rotation of the Midgut: A Report of Four Cases, Am. J. Digest. Dis. & Nutrition **4**:231, 1937.

of 15 days his vomitus contained unmistakable bile, and gastric lavage yielded bright green fluid with mucus. Up to this time the infant had been having one or two normal stools a day, but on the sixteenth day the return from an enema resembled old blood. Associated with these symptoms there occurred sudden and marked loss of weight with a temperature of 103.6 F., presumably resulting from dehydration, and the infant was admitted to the Babies Hospital. He weighed 3,850 Gm. and was active and hungry. The mucous membranes were dry, but the subcutaneous tissue was still elastic. No mass was felt in the abdomen, and no waves were seen. On roentgen examination the stomach was seen to be dilated, and it lay in the right side of the abdomen (fig. 20); the liver was on the left; the duodenum was dilated, and the proximal coils of jejunum occupied the left upper quadrant. There was delayed gastric emptying, with 50 per cent retention

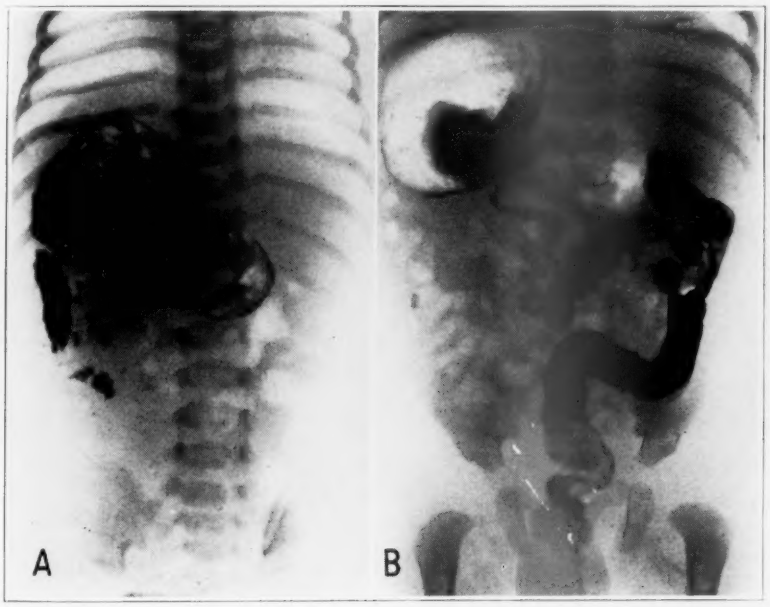

Fig. 20 (case 17).—Roentgenograms showing situs inversus abdominalis partialis. In *A*, taken one and one-half hours after an opaque meal was given, the stomach and the proximal coils of the jejunum are seen to lie on the right, while the heart is in its normal position. In *B*, taken after partial expulsion of a barium sulfate enema, the distal portion of the colon is seen to be in the normal position, the proximal and transverse portions being involved in the anomaly of rotation; a portion of the opaque meal given two days previously is still visible in the stomach.

after seven hours and incomplete evacuation after forty-eight hours, and the duodenum appeared enlarged at every examination. A barium sulfate enema showed the sigmoid flexure and the descending colon in normal position on the left; the transverse colon was in normal position approximately as far up as the midpoint of the abdomen, where there was a sudden curving back to the left; the cecum lay high in the left upper quadrant, with the tip of the appendix directed upward.

From this examination the diagnosis of situs inversus abdominalis was made, and the presence of obstruction at the third portion of the duodenum, with possibly other partial obstruction beyond, was inferred. In spite of graduated feedings and the administration of parenteral fluids, the patient continued to do poorly, with persistent bilious vomiting and the passage of small infrequent stools, some of which contained blood.

The infant was operated on at the age of 23 days. There was situs inversus of the stomach, of the portion of the intestine derived from the midgut, of the organs arising from it (liver, gallbladder and pancreas) and of the spleen. The descending colon and the sigmoid flexure were normally located on the left, but the transverse colon was doubled on itself at about its midpoint, so that the cecum lay on the left (fig. 21). The mesentery of the ascending colon was adherent to the jejunum at the point where it joined the duodenum, which caused the latter

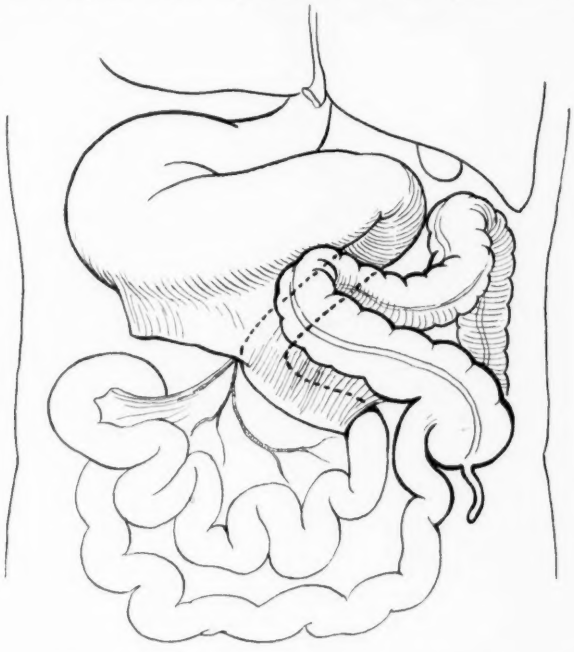

Fig. 21 (case 17).—Incomplete situs inversus abdominalis, with duodenal obstruction resulting from anomalies of rotation and associated peritoneal bands.

to be obstructed by kinking. The stomach was enormously dilated, the great omentum was poorly developed, and there were adhesions between the omentum, the transverse colon and the duodenum. The greater part of the jejunum and ileum lay in the right lower quadrant. After section of the adhesions the duodenal obstruction was relieved, and the transverse colon could be straightened out over the second portion of the duodenum. The cecum and the ascending colon were sutured to the parietal peritoneum on the right side of the abdomen; after the small intestine was rotated through 90 degrees counterclockwise it was possible to bring the third portion of the duodenum into contact with the posterior abdominal wall, this portion crossing from left to right behind the superior mesenteric artery and running downward and to the right to emerge beneath the terminal part of the ileum approximately at the region of the ileocecal junction.

Convalescence was uneventful except for some bilious vomiting during the first three postoperative days. The patient has remained in good health during the seven months which have elapsed since operation.

Pernkopf [66] in 1926 reviewed the literature of situs inversus partialis, and in 1928 he reported an additional case.[67] In 1932 Spitz [30] was able to find only 2 reported cases of situs inversus partialis abdominalis associated with mesenterium commune in which diagnosis was certain and 2 in which it was doubtful. Cases in which mesenterium commune does not occur are not nearly so rare. Oehlecker [16] described an example of the double anomaly in a physician who had experienced brief attacks of abdominal pain since childhood; at operation, at the age of 30 years, the stomach and two spleens were found lying on the right and the liver on the left, and the entire small intestine was twisted one and a half turns clockwise about its narrow mesenteric root. There were prominent bands and adhesions at the base of the mesentery in the region of torsion. The patient improved greatly, gaining 20 pounds (9.1 Kg.) within a short time after operation. In our case the volvulus of the small intestine constituted the lesser cause of duodenal obstruction, a greater part being played by the kinking of the duodenum due to the congenital peritoneal bands.

MALROTATION WITH HERNIA OF THE SMALL INTESTINE INTO A MESENTERIC POUCH

CASE 18.—William S., a twin, gained rapidly during the first ten weeks of life, being fed partly by breast and partly by bottle. The appetite was good, he regurgitated but slightly, and the stools were normal. Bilious vomiting commenced suddenly at the age of 10 weeks; this was associated with cessation of passage of stools and lasted for three days prior to the infant's admission to the hospital. When brought in he was in a state of collapse. The temperature was 102.2 F.; the abdomen was rigid and tender, but no masses were palpable. Operation was done on the day of the patient's admission.

Incomplete rotation of the large intestine was found; the cecum lay approximately in the midline and was attached by a long mesentery which was continuous with that of the terminal part of the ileum. In the angle between the cecum and the terminal part of the ileum there was a ballooned out pouch of mesentery in which practically the entire mass of small intestine was invaginated and held as in a wide-mouthed sack (fig. 22). The stomach and pylorus were normal; the duodenum was enormously dilated, with a diameter equal to that of the midportion of the stomach and with a thickened muscular wall. The terminal portion of the duodenum and the duodenojejunal flexure could not be readily brought into view, and a side to side duodenojejunostomy was performed.

66. Pernkopf, E.: Der partielle Situs inversus der Eingeweide beim Menschen; Gedanken zum Problem der Asymmetrie und zum Phänomen der Inversion, Ztschr. f. d. ges. Anat. (Abt. 1) **79**:577, 1926.

67. Pernkopf, E.: Ein neuer Fall von partiellen Situs inversus der Eingeweide beim Menschen mit besonderen Missbildungen am Herzen [Fall VI], Ztschr. f. d. ges. Anat. (Abt. 1) **87**:661, 1928.

The operative wound became infected, and eventration occurred eight days after operation. The patient died two days later. Autopsy showed a leak in the anastomosis, with surrounding peritonitis. A peritoneal band ran from the area of duodenal obstruction to the spine. The distended portion of the duodenum, 9 cm. in length, measured 3 cm. in diameter. The error of rotation of the intestines appeared as described in the operative note.

Lickley and Cameron [68] described a comparable instance of hernia into a mesenteric pouch associated with malrotation, and Haymond and Dragstedt's first case [4] was similar. Neff [69] reported an example in a girl of 14 years, whose symptoms preceded operation by only two days and whose small intestine was found to lie in a pocket, to the right of the spine, formed by the mesentery of the proximal part of the colon

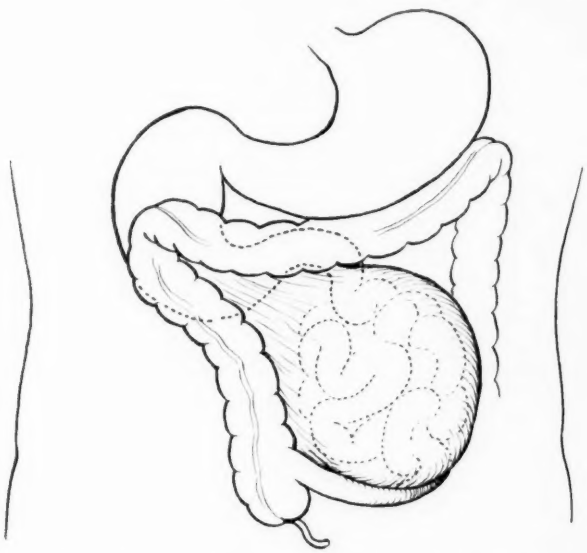

Fig. 22 (case 18).—Diagram of the anomaly. A large portion of the small intestine is enclosed in a pouch formed by the common mesentery of the terminal part of the ileum and the proximal part of the colon. There is an associated error of rotation and of peritoneal fixation.

anteriorly and the posterior abdominal wall behind. A large coil of ileum, which had escaped from the caudal end of the pouch, was obstructed by volvulus with rotation of 360 degrees counterclockwise. The duodenojejunal junction lay low down to the right of the vertebral column, and the root of the common mesentery of the part of the intestine originating in the midgut followed a short course at right angles to

68. Lickley, J. D., and Cameron, J.: Note on a Case of Abnormal Disposition of the Peritoneum, J. Anat. & Physiol. **41**:88, 1906.

69. Neff, G.: Hernia mesenterico-parietalis dextra mit Volvulus, Schweiz. med. Wchnschr. **67**:645, 1937.

its normal disposition, running from the right above to the left below. The condition in Neff's case differed from that in ours mainly because in the former partial fixation of the proximal part of the colon to its normal bed had taken place. Additional types of internal hernia associated with errors of rotation have been reported: for example, hernia into the lesser peritoneal cavity (Morton and Jones [60]) and through a defect in the mesentery (Ribadeau-Dumas and others [70]). As in case 17, the intestinal obstruction in our patient appeared to be caused by bands constricting the duodenum rather than by the associated anomaly.

REVERSED ROTATION WITH DUODENAL OBSTRUCTION

Cases of true reversed rotation are rare. In this condition the postarterial segment of the midgut precedes the prearterial segment in its return to the abdominal cavity from the umbilical cord, and the normal rotation of 270 degrees counterclockwise is replaced by one of 90 degrees clockwise, the transverse colon coming to lie behind the second portion of the duodenum. Truesdale,[71] writing in 1935, found only 11 cases in the literature and added 2 of his own. His tabulation did not include Gutiérrez' case,[44] reported in 1934, in which the diagnosis was verified by autopsy. Additional instances have been described by Andersen [72] and King.[18] The account of Hipsley's case [54] does not permit certain identification, but it is doubtful whether his is an example of true reversed rotation. The total number of indubitable cases which we have been able to find, then, is 16, to which may be added the following case.

CASE 19.—William S. was admitted to the Babies Hospital at the age of 12 years and 11 months. He had had digestive difficulties off and on almost all his life; they commenced with projectile vomiting at the age of 2 weeks. During the five months in which he was nursed, projectile vomiting appeared in recurrent attacks about one week apart. Improvement in this complaint followed weaning, though the patient remained somewhat difficult to feed. At about the age of 3 years he began to have frequent attacks of abdominal pain and lost some weight; at times he experienced nausea or vomited. Efforts to combat these symptoms on the basis of an existing tendency to constipation or from the standpoint of hypersensitivity to certain foods were not strikingly successful, and the patient continued to be underweight and below par physically. From the age of about 6 to 7 years he was free from acute distress. At 7 years, however, after a mild infection of the upper part of the respiratory tract he had a violent attack of bilious vomiting, with dehydration and sudden loss of weight which required parenteral adminis-

70. Ribadeau-Dumas, L.; Longuet, S., and Forget: Sténose duodénale, Bull. Soc. de pédiat. de Paris **34**:334, 1936.

71. Truesdale, P. E.: Retroposition of the Transverse Colon: Report of Two Cases, J. A. M. A. **104**:1697 (May 11) 1935.

72. Andersen, K. M.: Case of Retroposition of the Colon and Mesenterium Ileocolicum Commune with Torsion, Hospitalstid. **78**:911, 1935.

tration of fluids. This attack, which was labeled acidosis, lasted for about two weeks. Soon after this the tonsils and adenoids were removed, and the boy remained free from disturbing digestive symptoms for two years. A second severe attack of bilious vomiting and dehydration occurred at the age of 10 years, following overexertion and dietary indiscretion. During the ensuing four or five months one attack followed another in rapid succession, which resulted in considerable loss of weight and strength. Up to that time constipation had been constantly present; from then on, however, the patient stopped having formed stools, although at no time could he be said to have diarrhea. It was noticed that food did not appear in the stools until about ten days after ingestion. On one occasion bright red blood was seen in the stool. The patient was given a high protein, low roughage diet. Two weeks before admission to the hospital, after a long automobile ride, he began complaining of pain in the upper part of the abdomen, which came on an hour after a large meal was eaten. Vomiting was induced in an effort to control nausea, and for two days no food or fluid was given by mouth. Soon after the resumption of peroral feeding the epigastric pain and nausea recurred, so that the patient was forced to continue on a starvation regimen until admission, taking a solution of dextrose by rectum and small amounts of water and a solution of dextrose by mouth.

On admission the patient was emaciated, though not uncomfortable from thirst. He weighed 21.45 Kg. and measured 146 cm. in height. (Assuming that this height was normal for his age, he was about 40 per cent below the average in weight.) He was alert and cooperative and free from acute distress, though he referred to an intermittent sensation in the right upper quadrant which felt "like something trying to pass through, which gurgles, and then it goes." The temperature was 98.6 F., the pulse rate was 62 and the respiratory rate 20 per minute, and the blood pressure was 82 systolic and 70 diastolic. Physical examination disclosed only the signs of malnutrition and failed to explain their derivation. The blood count and the urine were normal, as were also the erythrocyte sedimentation rate and the stool. Reactions to the tuberculin and the Kahn test were negative. Whole blood values for nonprotein nitrogen and sugar and serum levels of calcium, phosphorus, cholesterol, chloride, carbon dioxide–combining power, albumin and globulin were all within normal limits. Gastric contents contained some free hydrochloric acid and a low normal amount of total acids; results of the bile test were positive. Fluoroscopic study of the gastrointestinal tract showed dilatation of the fundus of the stomach. The pylorus opened normally, allowing the opaque meal to enter a greatly dilated duodenum. An apparently complete obstruction existed at approximately the position of the duodenojejunal junction (fig. 23). Antiperistalsis was observed, and within a few minutes the duodenal contents were returned to the stomach. Roentgenograms taken after one-half, one, two and one-half and seven and one-half hours failed to show passage of duodenal contents beyond the point of obstruction. The valvulae conniventes appeared to be hypertrophied. After twenty-four hours flecks of opaque material were seen scattered throughout the small intestine, with a small bolus lying in the tip of the cecum; the duodenal obstruction was therefore not absolute or at least not constant. Fluoroscopic study after a barium sulfate enema revealed redundancy of the transverse colon, with numerous extra folds; the cecum was situated in the left half of the abdomen. Several times during observation prior to operation the patient vomited from 600 to 800 cc. of bile-stained material. He was prepared for operation by daily parenteral injection of 2,400 cc. of a solution of sodium chloride for three days and two transfusions, 250 cc. being given with each.

Nine days after admission operation was performed with a right upper paramedian incision. The actual identification of the different loops of intestine proved rather difficult. A large loop, which at first appeared to be transverse colon, lay across the upper part of the abdomen; later this was found to be the proximal part of the colon, with the ileum entering the cecum from the right and below (fig. 24). Posteriorly to this loop the jejunum emerged from a retroperitoneal tunnel, which caused obstruction by kinking. The small intestine, in addition, was rotated through 180 degrees clockwise in a volvulus which twisted its long mesentery about the axis of the superior mesenteric vessels, producing traction on the mesenteric root. The cecum and the ascending colon were brought over to the right lower quadrant, and the cecum was attached to the parietal peritoneum there with interrupted sutures of chromic catgut, which permitted the volvulus to be reduced.

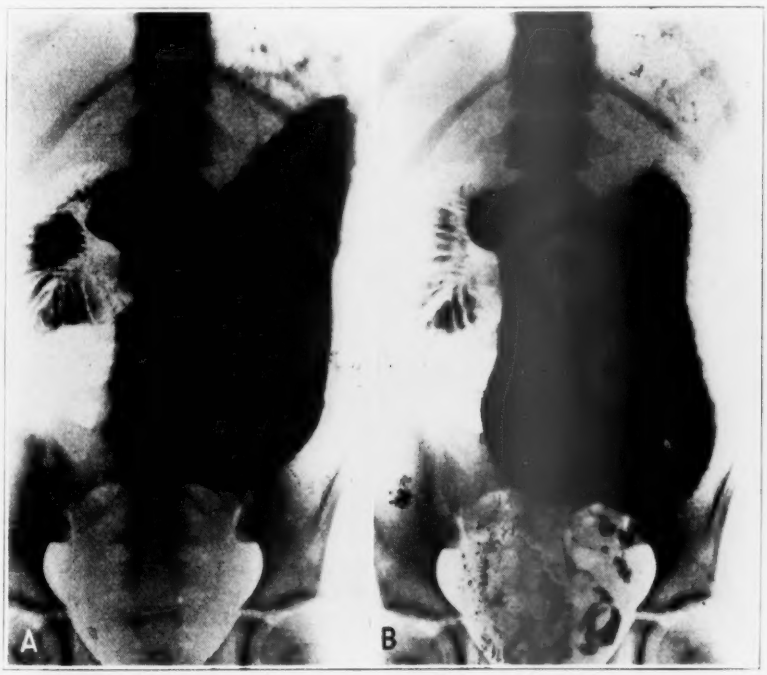

Fig. 23 (case 19).—*A*, roentgenogram taken fifteen minutes after an opaque meal was given. Note the prominence of the valvulae conniventes in the duodenum. *B*, roentgenogram taken twenty-four hours later. Only a small part of the meal has passed the point of obstruction.

It was then found that the duodenum coursed anteriorly to the transverse colon, which was snugly attached to the posterior abdominal wall at the point where the duodenum passed in front of it. The reversed rotation could not, of course, be corrected. The sharp angulation at the duodenojejunal junction was straightened out to some extent by section of peritoneal bands maintaining it, and the patient was given another 250 cc. of blood by transfusion immediately after operation.

Convalescence was uneventful. The patient did not vomit after operation, and because of his poor nutrition he was fed earlier than would be attempted in other cases of this kind. In a few days he was on a liberal diet, enjoying his meals as he

had not done in years and taking many foods which had been alleged to make him sick. On leaving the hospital, three weeks after operation, he had gained 4.15 Kg. above his weight on admission, and he added 4.5 Kg. in the following ten days. Six and a half months later he was still entirely free from digestive disturbance, looked perfectly healthy and had gained 20.91 Kg. (46 pounds) since operation.

The intermittent nature of the patient's digestive symptoms combined with a familial consciousness of "indigestion," from which both

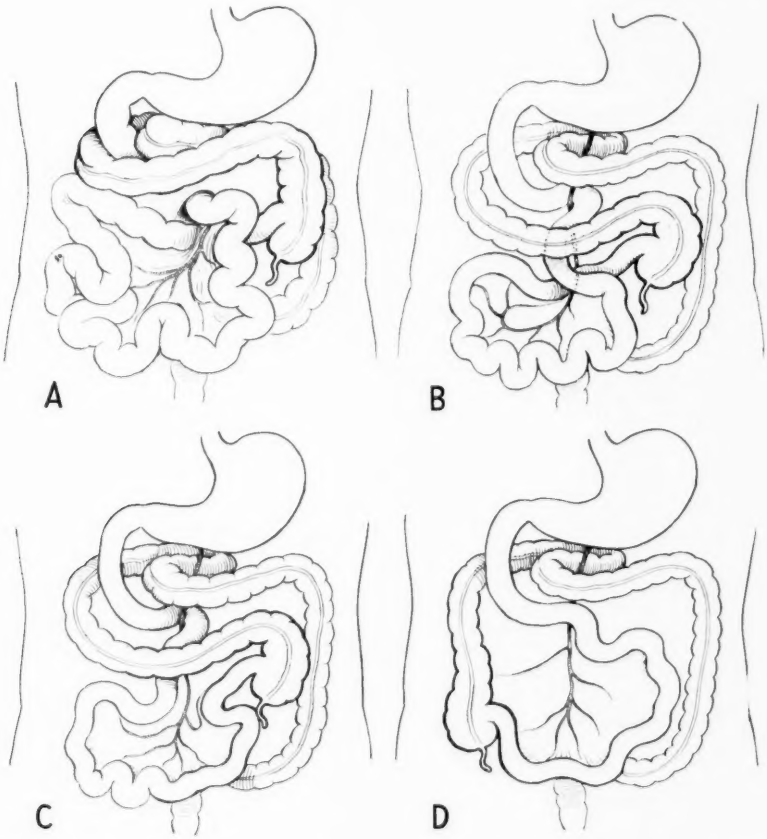

Fig. 24 (case 19).—Diagram of the pattern of the intestine: *A*, as found at operation; *B*, after partial reduction of volvulus of the small intestine; *C*, after full reduction of the volvulus and *D*, after surgical fixation of the proximal part of the colon. The reversal of intestinal rotation is shown by the fact that the duodenum passes anteriorly to the transverse colon and to the superior mesenteric artery. The kink in the transverse colon could not be corrected surgically.

parents and a sister suffered from time to time, to force on him a strong functional psychic element in the pathogenesis, as well as in the interpretation, of symptoms. Nevertheless, it was abundantly clear from the objective findings, particularly those developed by roentgen examina-

tion, that at the time of admission to the hospital he was suffering from acute obstruction of organic origin. This idea was strongly supported by the maintenance of unimpaired appetite in the presence of bilious vomiting. Since previous attacks of a similar nature had resolved themselves under expectant treatment, it is reasonable to suppose, as suggested in the discussion of case 5, that this patient's crises of vomiting and abdominal pain coincided with volvulus of the portion of intestine originating in the midgut and that the rather sudden though incomplete amelioration of distress derived from spontaneous resolution of volvulus. The background of less dramatic complaints—the failure to gain, the slow passage of food through the alimentary tract and the fear of dire consequences from eating a full meal—may well represent the more fixed element of the obstruction found, the kinking at the duodenojejunal junction. In this case one cannot ascribe any symptoms at all to the reversed rotation itself.

MALROTATION CAUSING MELENA IN CHILDHOOD

CASE 20.—Theodore A. was admitted to the hospital at the age of 8 years because the stools had been tarry for one week. He was known to have congenital malformation of the heart. In infancy he had been subject to digestive upsets, with colic and abdominal distention and occasionally with diarrhea. Since the age of 5 years he had had frequent belching in the morning and spells of vague abdominal pain. One week before admission he vomited some whitish material, and from then on he complained repeatedly of pain in the upper part of the abdomen. The stools became tarry, and rapidly progressing anemia developed. There was no bleeding from any other source, and the appetite remained unimpaired. The patient weighed 27 Kg., was pale and had rather flabby musculature. The heart was not enlarged; a moderately prominent systolic murmur was audible all over the precordium, being loudest in the third and fourth interspaces to the left of the sternum; the aortic second sound was fainter than the pulmonic. The blood pressure was 106 systolic and 70 diastolic. The abdomen was somewhat distended, and in the midline a cord could be felt from the umbilicus to the pubis. Rectal examination showed normal conditions except for the return of tarry fecal material, which gave a positive reaction to the guaiac test. The hemoglobin level was 10.2 Gm. per hundred cubic centimeters. Red cells numbered 2,550,000 per cubic millimeter. The leukocyte count, platelets, coagulation time and clot retraction were normal. Tuberculin and Kahn tests gave negative results. The patient was watched for nineteen days, during which he was afebrile except for a reaction after transfusion on the thirteenth day. The hemoglobin level was raised to 11.9 Gm. per hundred cubic centimeters and the red cell count to 4,660,000. Roentgen examination of the alimentary tract showed the cecum to lie in the left iliac region, with the proximal part of the colon practically in the midline; the sigmoid flexure was long and redundant, and the entire colon was somewhat large. The preoperative diagnosis was persistent Meckel's diverticulum.

At operation failure of fusion was found between the great omentum and the transverse mesocolon. The cecum was movable and redundant. Only the

first portion of the duodenum was retroperitoneal, the duodenojejunal flexure being hitched up in a pocket in its mesentery (fig. 25). There were numerous large varices of the superior mesenteric vein and its branches, some of them attaining the diameter of one's little finger; these constituted the obvious source of bleeding. No Meckel diverticulum was found. The bands at the duodenojejunal junction were freed to some extent, and the abdomen was closed without further attempt at surgical correction.

The postoperative course was smooth, the anemia disappeared, and the patient remained free from symptoms for the following two years, during which he was kept under observation. His attacks of abdominal pain did not recur.

The circulatory embarrassment caused by obstruction of the venous return at the mesenteric root in the presence of errors of intestinal rotation has been repeatedly observed,[73] but to our knowledge this is

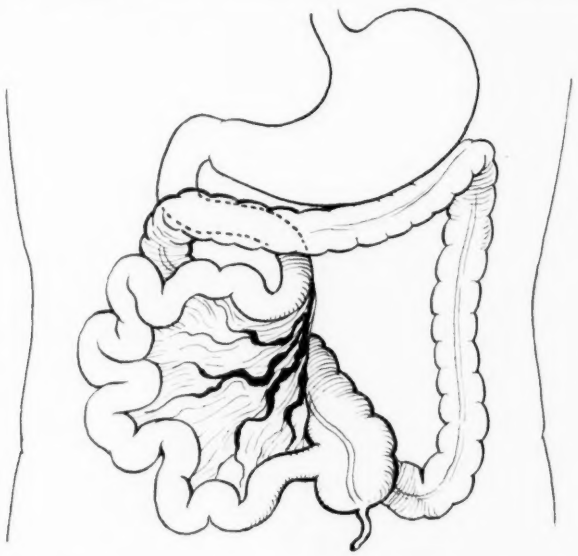

Fig. 25 (case 20).—Varices of the superior mesenteric vein and its branches associated with anomalous rotation and fixation of the portion of intestine derived from the midgut.

the only case in which gross intestinal bleeding constituted the chief complaint. Patients with hemorrhage from Meckel's diverticulum occasionally suffer attacks of abdominal pain as well, so that the error in preoperative diagnosis is the more readily explicable, in view of the relatively common occurrence of the latter anomaly. Obstruction of the superior mesenteric vein and its tributaries in association with abnormality of intestinal rotation but in the absence of volvulus of the portion of intestine arising from the midgut is distinctly rare. At the time of operation the freeing of bands at the mesenteric root did not effect an

73. Gardner and Hart.[5] Morton and Jones.[60]

immediate improvement in the circulation of the bowel, but the patient's freedom from symptoms permits one to hope that the remedy was adequate.

COMMENT

It is obvious that not all errors of rotation of the midgut produce a sufficient degree of obstruction of the alimentary tube or of its circulation to attract attention. At the same time, it is equally plain that in many of the situations in which obstructive symptoms occur the life of the patient is threatened unless relief is sought. Of our 20 patients with anomalies of the type under discussion, in 13 volvulus was found at operation. Some of the authors writing on this subject have laid emphasis on the part played by volvulus in producing the symptoms of obstruction, while others have stressed the kinking and compression of the duodenum by congenital peritoneal bands and the constricting effect of other malformations of the mesentery. Our series includes examples of all of these types, and we wish to point out that preoperative differentiation among them is always difficult and often impossible. But although the anomaly of rotation may not lend itself to surgical correction, relief of the obstruction is invariably possible, and it is consequently of the utmost importance for the pediatrician to be aware of the implications of the accompanying syndrome and to recognize its dependence on an organic, structural abnormality, so that adequate therapeutic measures may be taken in time, for delay may prove costly. It is the pediatrician who is concerned, for in the majority of cases symptoms develop in the first few days of life (they appeared within the first two days in 65 per cent of our cases and within the first two weeks in 85 per cent) and it is his responsibilty to seek the assistance of a competent surgeon.

Duodenal obstruction dominates the clinical picture, with bilious vomiting and progressive loss of weight as its cardinal symptoms. The rare exceptions noted in the cases presented here may for the moment be ignored. With obstruction from volvulus or from constriction of the intestinal lumen from the outside by tight peritoneal bands, the degree of ileus is usually incomplete, and stools are passed. Only a little more than half of our patients had sufficiently marked constipation to attract attention. Meconium is expelled by these patients even when vomiting appears after the first feeding taken; as in the case of patients with developmental atresia of the duodenum or of the upper part of the jejunum, the fact that meconium is passed is not a valid sign of patency of the alimentary tract. After the transition from meconium to fecal stools has occurred, it is always worth while to attempt to compare fecal volume with the volume of the food ingested in order to determine the completeness of the obstruction, but in actual practice

such observations are fogged by lack of regularity or measurableness in the severity of vomiting. The course of the weight curve is a more practical guide.

In cases in which symptoms occur during the first few days of life, differential diagnosis includes "functional vomiting," congenital intrinsic obstruction of the alimentary tube, pyloric stenosis, intracranial lesions and parenteral or enteral infections. By the term "functional vomiting" we mean to indicate the type of condition for which no organic cause is found and which clears up spontaneously within a few days. It is familiar to pediatricians and is not easy to define in physiologic terms. Not infrequently the tendency to vomit, coinciding with the administration of the first few feedings, attains conspicuous proportions and, by prolonging the neonatal loss of weight, raises a serious diagnostic problem. Although time eventually reveals its true significance, we find that we have come to rely more and more on roentgen examination to dispel the doubts which must arise when this type of vomiting persists to an appreciable degree. As we have resorted to this diagnostic aid with increasing promptness after the appearance of symptoms, our proportion of positive results—of findings which show the presence of an organic obstruction—has progressively diminished. Perhaps this merely reflects our mounting awareness of the importance of fluoroscopic study after an opaque meal in the establishment of early diagnosis and in the localization of obstruction. Certainly one cannot readily do without this examination. Functional vomiting is bilious but rarely and then only temporarily; the persistence of bile in the vomitus points strongly to organic obstruction. We have not found that this early form of transitory and essentially unimportant vomiting is greatly influenced by the type of feeding given, whether breast or bottle, nor has it close correlation with the mother's clinical status before or during labor.

Intrinsic developmental obstructions occurring at the level of the esophagus are readily distinguished, but those lying beyond the pylorus offer more difficulty. When the clinical syndrome of high intestinal obstruction or of duodenal obstruction below the papilla of Vater is associated with the roentgen picture of complete block, with dilatation of both duodenum and stomach above it, the chances are great that the cause lies in developmental atresia which arises from failure of recanalization of the alimentary tube. In our group of cases in which anomalies of rotation occurred we observed but 1 instance of complete obstruction due to volvulus or to peritoneal bands, while during a comparable period 5 patients came to the hospital in whom duodenal atresia was demonstrated either in life or at autopsy. Here, of course, duodenojejunostomy is the remedy. When the degree of obstruction is incomplete, the differential diagnosis between stenosis of intrinsic

origin and constriction from volvulus or from peritoneal bands can scarcely be made without surgical exploration, although the roentgen demonstration of a jejunum on the right or of failure of migration of the cecum will argue that the obstruction is from without. Transition from an incomplete to a complete block may be regarded as a strong hint of volvulus of the portion of intestine derived from the midgut loop.

The onset of vomiting in cases of congenital hypertrophic stenosis of the pylorus is usually deferred until after the first week of life, and the vomitus rarely if ever contains bile; yet it is possible for the disturbances secondary to errors of rotation to simulate closely the clinical picture of pyloric stenosis. The palpation of a pyloric mass in some of our cases, in the absence of hypertrophy of the pylorus, has already been commented on, and the occurrence of prominent gastric peristaltic waves is an indication of the presence of an obstruction rather than of its location, since waves are seen with either a pyloric or a duodenal block. We believe that errors in diagnosis are unlikely if one keeps both possibilities in mind in studying cases of early vomiting; when doubt persists after the clinical evidence has been weighed, it can promptly be dispelled by resort to fluoroscopic study of a barium sulfate meal. A mistake in diagnosis is costly here only if conservative therapy is unduly prolonged.

With some of the intracranial lesions resulting from birth trauma or hemorrhage and with the forms of meningitis arising out of early sepsis, especially those caused by systemic infection with organisms of the Escherichia group, vomiting may be the most prominent symptom. One can usually obtain sufficient supporting evidence in these cases to demonstrate that the primary cause of vomiting lies outside the gastrointestinal tract. With the exception of meningitis, practically all of the parenteral infections appearing in the neonatal period and all of the enteral infections, including the form of diarrhea of the newborn now thought to be caused by a filtrable virus, commonly cause marked diarrhea and relatively mild vomiting. With the obstructions caused by errors of rotation of the intestinal tract, vomiting is by far the more prominent symptom. The one important caution to be expressed is that the passage of starvation stools composed mainly of bile-stained mucus should not be mistaken for true diarrhea.

When the picture of intestinal obstruction develops at a later age, one must consider intussusception, internal hernia, volvulus of a limited portion of the intestine and obstruction caused by tumors. Some of these conditions have a characteristic clinical picture; some can be identified by adequate use of roentgen technics, and others, only after surgical exploration. It will be recalled that some of our older patients

were accused of having gastritis, appendicitis, cyclic vomiting, acidosis, hypersensitiveness to particular foods, absorption from a focus of infection, emotional instability or psychogenic disturbance. If one but keeps in mind the possibility that anomalies of intestinal rotation may be at the basis of symptoms and investigates the question roentgenographically, not only after the administration of an opaque meal but also after giving a barium sulfate enema, the opportunity is at hand for obtainting brilliant results by surgical intervention.

The patient whose chief complaint was loss of blood by the bowel led us too easily into a diagnostic error. After intussusception, volvulus, ulcerative colitis and tuberculous enteritis had been excluded, when sigmoidoscopic study had failed to reveal the presence of a rectal polyp or an impacted foreign body, and when it was shown by appropriate study that the boy was not suffering from any general blood dyscrasia or from Henoch's purpura, the bleeding was inferred to be coming from a persistent Meckel's diverticulum. The true diagnosis was discovered only at operation.

Of our 20 patients, 18 were operated on; of these, 6 died. The causes of death we have interpreted as follows: excessive delay in surgical intervention in 2 cases (1 and 13); operative shock in 1 case (14); inadequate relief of obstruction in 1 case (15) and postoperative infection in 2 cases (10 and 18). Of the last 2 cases, in 1 the patient had a disseminated infection which probably originated in the operative wound; in the other, a leak in the intestinal anastomosis was the source of peritonitis. Both of these patients suffered postoperative exenteration, one seven days and the other eight days after operation. On the other hand, another patient (case 9) survived this complication. In the decade 1920-1929, 4 patients were operated on, with 3 deaths; since then 14 patients have been operated on, with 11 recoveries. Ladd [11] and others reported a comparable improvement in surgical mortality. One of our patients experienced 2 proved episodes of volvulus and has had a number of subsequent attacks which suggested the occurrence of volvulus with spontaneous resolution. With this exception, all of the patients surviving have since operation remained free from the symptoms which originally brought them to the hospital, as long as we have been able to follow them. None has displayed intractable rickets, which was reported by Beutel and Nonnenbruch,[74] or other hazards of rapid growth after operation.

In the therapy of these anomalies, the preparation of the patient for operation by replacement of water and electrolytes lost during the pre-

74. Beutel, A., and Nonnenbruch, W.: Infantilismus mit Zwergwuchs bei Duodenalstenose und Wachstum mit Rachitis nach Gastroenterostomie, Med. Klin. **32**: 765, 1936.

ceding period of vomiting and starvation has been proved to be of signal importance. Transfusions of small volume are also helpful. We have not found that the administration of radiopaque material for diagnostic purposes adds materially to the operative difficulty or risk, provided care is taken to empty the stomach and the lower part of the bowel before operation.

The surgeon will often find the first confirmation of his suspicion of an anomaly in the rotational process in failure of fusion between the great omentum and the mesentery of the transverse colon. One can seldom visualize the existing abnormalities properly without delivering the mobile portions of the intestinal tract outside of the operative wound. A volvulus about the root of the mesentery then becomes plainly visible and is readily reduced. As Ladd [75] has cogently emphasized, it is essential in all cases of errors of rotation, whether volvulus is found or not, to visualize the duodenum so as to be prepared to relieve it of obstructing peritoneal bands. We have generally made an adequate approach by raising the transverse colon and moving the small intestine downward and to the right, though Morton and Jones [60] stated that they advocated detaching the proximal portion of the colon from its bed and mobilizing it to the left, so as to gain a clear view of the proximal, as well as of the terminal, portion of the duodenum. The corrective procedures to be used must be adapted to the requirements of each case. As a rule, duodenojejunostomy and other anastomotic operations are unnecessary unless the anomaly of rotation is accompanied by intrinsic obstruction, as in case 14 and presumably in case 15. The mere untwisting of volvulus and section of constricting bands are usually effective in relieving the obstruction. On the basis of a limited experience, we believe that as a preventive device the surgical fixation of the cecum and the proximal part of the colon in their proper beds is a safe procedure and should be undertaken if the patient's condition warrants it, with the expectation that it will abolish the tendency to recurrence of volvulus of the section of intestine derived from the midgut or of large portions of it.

In the first few days after operation, the fluid requirements are met almost entirely by parenteral administration of a solution of sodium chloride. Feedings are resumed slowly, with gradual increase of the volume of intake. It the case of young infants, we have found it convenient to use the routine employed postoperatively in cases of pyloric stenosis, breast milk being fed in graduated quantities, so that the requirements for maintenance and growth are attained approximately at the end of one week. Bilious vomiting during the first two or three days after operation is not uncommon and does not necessarily denote inadequate surgical release of the obstruction.

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75. Ladd, footnotes 11 and 61.

SUMMARY

Anomalies of developmental rotation of the intestinal tract, specifically of that portion of it which is supplied by the superior mesenteric artery, may cause symptoms of obstruction of the lumen of the intestine or of its venous return. We have reported 19 cases in which the patients presented the syndrome of organic ileus, most of them with a clearcut picture of duodenal obstruction, and 1 case of gross intestinal hemorrhage, all traceable to errors of intrauterine development of the midgut.

The cause of intestinal obstruction may lie in volvulus of the entire portion of intestine which arises from the midgut loop or of a large section of it, in the persistence of peritoneal bands which distort and constrict the duodenal channel or in combinations of these. Symptoms are likely to occur within the first few days of life. In some instances, however, there is a delay in their appearance, and in some, the symptoms may ameliorate and disappear spontaneously, only to return at a later age. We have reason to believe that spontaneous improvement in these cases often denotes that a loose twist of the intestine has resolved itself. Such episodes may be frequently repeated and may give rise to a serious diagnostic problem. In all cases of duodenal obstruction and in those of "periodic vomiting" as well, the possibility of their causation by anomalies of intestinal rotation should be investigated by appropriate study, especially by proper use of roentgen technics.

Recognition of these conditions and of the physiologic disturbances which accompany them has led in recent years to a significant improvement in the results of their surgical correction, not only in our hands but in the hands of others who have reported their experiences. In the attainment of this end, the cooperation of pediatrician, roentgenologist and surgeon has played a significant part.

Correspondence

METHOD OF ADDING APPLE TO MILK FORMULAS

To the Editor:—Since publication of the paper on addition of apple to the diet of infants (Reithel, F. J., and Manville, I. A.: Advantages of Adding Apple to Milk Formulas, Am. J. Dis. Child. **56**:237 [Aug.] 1938) I have received inquiries as to where the apple powder may be obtained and how it is used. In regard to the first question, Appella apple powder can be obtained through dispensers of drugs. It is being distributed by the Frederick Stearns Company, of Detroit.

The second question requires a more detailed answer. If the babies' formula is being built up from cow's milk, we use a good brand of evaporated milk, which is diluted to twice its volume with water containing 10 per cent apple powder. The water is prepared by placing 2 moderately heaped teaspoonfuls of apple powder in an 8 ounce (237 cc.) container. Water is added slowly, and the mixture is constantly stirred. The formula thus contains 5 per cent apple powder. This is the maximum amount which can be added without interfering with the passage of the formula through the opening in the rubber nipple. This formula is administered according to the usual routine.

For older children and adults, all food is withheld for three to four days, during which an 8 ounce glass of water containing 10 per cent apple powder is administered at three to four hour intervals. At the end of this period the transitional diet is started. Custards that have been prepared with milk containing 5 per cent apple powder and gelatin desserts made with water containing 15 to 20 per cent apple powder are fed. These foods, together with apple sauce or baked apple, occupy a rather prominent place in the menu for two or three days after the discontinuation of the apple powder water. Buttermilk and cottage cheese are added at times. Protein foods are restored to the diet last and with caution.

We have had just as good results from this therapy with older children and adults as with infants. This is particularly true with those who have the intestinal upsets commonly known as intestinal influenza.

Ira A. Manville, M.D., Portland, Ore.

News and Comment

GENERAL

The E. Mead Johnson Award for Research in Pediatrics.—At the Annual Meeting of the Academy of Pediatrics the offer of Mead Johnson & Co. to establish the E. Mead Johnson Award for Research in Pediatrics for ten years was accepted by the Academy. A Committee on Awards was appointed, consisting of Drs. Joseph Brennemann, Chicago; Irvine McQuarrie, Minneapolis; Oscar M. Schloss, New York; Edwards A. Park, Baltimore, and Borden S. Veeder, St. Louis (chairman). The committee announces that the following rules and regulations will govern the award:

1. Two awards, one of $500 and one of $300, will be awarded each year at the annual meeting of the Academy of Pediatrics.

2. The award will be made for research the report of which was published during the previous calendar year.

3. There is no limitation as to the type or scope of research except that it must be in the field of pediatrics.

4. The award is limited to workers in the United States and Canada.

5. The award is limited to investigators who graduated not more than fifteen years before the publication of the reports on their work.

6. There is no restriction as to the journal of publication.

The Committee interprets rules 2 and 3 as follows:

The award in 1939 will be given for research the report of which was published during the period from Jan. 1 through Dec. 31, 1938, by a graduate of 1923 or a later year. The award in 1940 will be given for research reported during the interval from Jan. 1 through Dec. 31, 1939, by a graduate of 1924 or a later year, and so on for subsequent years.

Heads of departments and of hospital services are requested to call attention to investigations which meet the requirements of the award and in particular to research work in the field of pediatrics published in other than pediatric journals. At present communications should be addressed to the chairman.

American Board of Pediatrics.—The American Board of Pediatrics will hold examinations during 1939 as follows: on Tuesday and Wednesday, April 25 and 26, in New York (appointments for this examination must have been made before Dec. 26, 1938); on Tuesday, May 16, in St. Louis, during the meeting of the American Medical Association (appointments for this examination must have been made before Jan. 16, 1939), and on Wednesday, Nov. 15, in Cincinnati, before the annual meeting of the American Academy of Pediatrics (appointments for this examination must be made before July 14, 1939).

SOCIETY NEWS

American Orthopsychiatric Association.—The sixteenth annual meeting of the American Orthopsychiatric Association, an organization for the study and treatment of behavior and its disorders, will be held at the Commodore Hotel, Lexington Avenue and Forty-Second Street, New York, on Feb. 23, 24 and 25, 1939. Dr. Norvelle C. LaMar, 149 East Seventy-Third Street, New York, is secretary.

DEATHS

Dr. T. Wingate Todd, professor of anatomy at Western Reserve University and director of the Brush Foundation, died of heart disease on December 28, at the age of 53 years. His work on the growth and development of the child is regarded by many as the outstanding contribution to that subject.

Dr. Lucy Porter Sutton, of New York city, died on December 23 of acute leukemia. Dr. Sutton had been an active worker in pediatrics for many years and was instructor of diseases of children at the College of Physicians and Surgeons, Columbia University. At the time of her death she was secretary of the Section on Pediatrics of the New York Academy of Medicine.

Dr. Sutton was well liked and an excellent worker in her chosen field. Her loss is greatly to be regretted.

Dr. John Signorelli of New Orleans, La., died on December 13, at the age of 49 years. Dr. Signorelli was medical director of the department of hygiene and child welfare of the Orleans Parish public school system. He was also professor of pediatrics at the Medical School of the Louisiana State University.

CORRECTION

In the article by Dr. Howard L. Alt entitled "Iron Deficiency in Pregnant Rats: Its Effect on the Young," in the November issue (AM. J. DIS. CHILD. **56**:975, 1938), the expression in parentheses in the third line from the top of page 983 should read "about 0.5 to 0.6 mg." instead of "about 0.5 to 6 mg."

Obituaries

RUSSELL STURGIS ROWLAND, M.D.
1874—1938

Russell Sturgis Rowland, a pioneer in the practice of pediatrics in Detroit, died on Sept. 28, 1938. Dr. Rowland was born in Philadelphia in 1874; he received his academic and medical degrees from the University of Michigan. After four years in the South Department of the Boston City Hospital, in the Children's Hospital and in the Boston Lying-in Hospital, he began the practice of pediatrics in Detroit. He became one of the organizers of the Detroit Milk Fund and interested himself in various aspects of child welfare. His activity in the practice of pediatrics covered more than thirty years. During his later years he engaged in investigative work, chiefly in the field of lipoid metabolism, receiving wide recognition for his studies. His chapters on the subject were included in "The Oxford Medicine" [1] and in Brennemann's "Practice of Pediatrics." [2] He was awarded the Silver Medal of the American Medical Association for his contributions in this field, and he received the honorary degree of Master of Science from his alma mater in 1936 in recognition of his accomplishments. He was a member of many professional societies, including the American Academy of Pediatrics and the American Pediatric Society. When illness had already claimed him, he did not rest with a sense of accomplishment on past efforts well performed but even then embarked on the investigations which were to bring him international recognition, actuated only by the desire to contribute to scientific knowledge and by love of the profession to which he had dedicated himself.

Dr. Rowland's career demonstrated the compatibility of scientific investigation and household practice. He was a man of varied interests. He took great delight in gardening and was especially interested in the cultivation of many varieties of iris. He was a beloved physician and a good citizen. His kindly presence and wise counsel will be missed in many circles.

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1. Rowland, J. S.: Anomalies of Lipid Metabolism, in Christian, H. A., and Mackenzie, J.: Oxford Medicine, New York, Oxford University Press, 1936, vol. 4, pt. 1, chap. 7 A.

2. Rowland, R. S., and Jaffé, R. A.: Constitutional Disturbances of Lipoid Metabolism and the Reticulo-Endothelial System, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 3, chap. 23.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

THE MUCOID PHASE IN DISSOCIATION OF THE GONOCOCCUS. P. J. ALMADEN, J. Infect. Dis. **62**:36 (Jan.-Feb.) 1938.

Encapsulated forms of gonococci were obtained from seven of eight strains that were studied. Except for the presence of a capsule, these strains were identical morphologically with the parent strains. The fermentative powers of the M phase paralleled those of the S phase. The organisms were as fastidious in their cultural requirements as were the original strains. The mucoid type of colony could be most easily distinguished from the S type of colony by fishing the colony with an inoculating needle.

TOOMEY, Cleveland.

THE TOXICITY OF YOUNG CELLS OF SALMONELLA PARATYPHI A AND B WHEN LYSED BY BACTERIOPHAGE. R. E. GORDON and C. N. STARK, J. Infect. Dis. **62**:45 (Jan.-Feb.) 1938.

The data reported indicate that young cells of Salmonella paratyphi A and B, the autolyzed mature cells of which produce a toxic substance, do not liberate a filtrable toxic material in amounts detectable by the methods employed in this study.

TOOMEY, Cleveland.

RATE OF DISAPPEARANCE OF CRYSTALLINE EGG ALBUMIN FOLLOWING ITS INTRAVENOUS INJECTION. H. B. KENTON, J. Infect. Dis. **62**:48 (Jan.-Feb.) 1938.

As shown by the average rate for 16 rabbits, crystalline egg albumin introduced intravenously disappears from the blood with rapidity: 85 per cent in one hour, 94.4 per cent in two hours and 99.6 per cent in twenty-four hours.

TOOMEY, Cleveland.

STUDIES UPON MINUTE HEMOLYTIC STREPTOCOCCI: IV. FURTHER OBSERVATIONS ON THE DISTRIBUTION OF ORDINARY AND MINUTE BETA HEMOLYTIC STREPTOCOCCI IN THE NORMAL AND THE DISEASED HUMAN BEING. P. H. LONG and E. A. BLISS, J. Infect. Dis. **62**:52 (Jan.-Feb.) 1938.

Minute hemolytic streptococci of the beta type were found in cultures of material from the rhinopharyngeal regions of 12 per cent of normal persons from whose throats material was occasionally taken and cultured. In a group of normal adults in whose case at least 11 consecutive cultures were made at weekly intervals, the incidence of these organisms was 23 per cent.

The minute organisms were rarely isolated from patients ill with chronic diseases, acute infections of the upper part of the respiratory tract or acute streptococcic infections, such as scarlet fever or streptococcic tonsillitis.

Children admitted to the clinic of the Harriet Lane Dispensary showed an incidence of 15 per cent when single cultures were studied for the presence of these minute organisms.

These streptococci were found in the rhinopharyngeal mucus of 55 per cent of patients ill with rheumatic fever or its sequelae.

These organisms were found in the rhinopharyngeal material of 96 per cent of 48 patients suffering from diffuse glomerular nephritis of type A and in that of 40 per cent of 37 patients ill with diffuse glomerular nephritis of type B. Only

3 per cent of 33 patients who had recovered from glomerular nephritis showed these minute organisms in cultures of material from the rhinopharynges.

The authors' observations confirm and extend the earlier findings of Longcope and his associates that beta hemolytic streptococcic infection is of causal importance in diffuse glomerular infection of type A. TOOMEY, Cleveland.

Metabolism; Infant Feeding; Milk and Other Foods

AN OVERSIZED INFANT WITH EARLY DENTITION. M. SCHACHTER-NANCY, Lattante **8**:491 (Aug.) 1937.

The infant, a boy, weighed 10½ pounds (4,763 Gm.) and had two teeth at birth. At the age of 8 months, he weighed 24 pounds 11 inches (11,198 Gm.) and was 30¾ inches (78 cm.) tall; this is the size of a child aged 1½ years. The mother was obese, weighing 167 pounds (75.7 Kg.), and had had two previous miscarriages, although a serologic study of her blood gave negative results. The author discusses the possible causes of this child's obesity, large size and early dentition from the point of view of the endocrine system—especially, the pineal, pituitary and thyroid glands—and from that of the vegetative nervous system and possible neurotrophic infections, such as syphilis. HIGGINS, Boston.

NONSPECIFIC INFANT FEEDING IN EARLY INFANCY. C. P. MONTAGNA and A. A. RIMOLDI, An. Soc. de puericultura de Buenos Aires **3**:25 (Jan.-March) 1937.

The authors stress the need of proper feeding of infants from the standpoint of quantity and quality of the food and from that of adaption and assimilation of the food by the infant. Each of these four factors must be considered. They review the general principles of infant feeding. HERRON, Monroe, La.

NUTRITION OF THE NURSING MOTHER. H. I. BURGOS and P. J. VERNOCCHI, An. Soc. de puericultura de Buenos Aires **3**:77-83 (April-June) 1937.

The authors review the normal constituents of an average diet and suggest that a nursing mother eat a normal diet, adequate in minerals, vitamins and calories. HERRON, Monroe, La.

BREAST MILK MIXTURES FOR SICK INFANTS. S. I. BETTINOTTI, Arch. argent. de pediat. **8**:1131 (Nov.) 1937.

Bettinotti describes milk mixtures for sick infants in which human milk was used. Mother's milk was mixed with cow's milk, protein milk, flour and different sugars. He again emphasizes the advantages of mother's milk as the most natural form of feeding for infants, especially sick ones. SCHLUTZ, Chicago.

p_H OF BREAST MILK. O. POLLERI and R. REGO, Arch. argent. de pediat. **8**:1278 (Dec.) 1937.

Polleri and Rego present studies of the hydrogen ion concentration in breast milk by the potentiometer method. Determinations of p_H were made on 2,000 samples from 30 women. The values varied from 7.07 to 7.61, with an average of 7.34. A sample twenty-four hours old with an increased bacterial count had a p_H of 6.26; a fresh sample, a p_H of 7.17.

The p_H determinations reveal any adulteration, the grade of preservation, a difference from cow's milk (p_H 6.5) and an absence of changes in the milk during the menstrual period. SCHLUTZ, Chicago.

NUTRITIONAL DISTURBANCES. A. WIEDERHOLD, Rev. chilena de pediat. **8**:616 (Nov.) 1937.

Wiederhold claims that nutrition is still the basic problem in pediatrics and that an absolutely optimal artificial feeding has not been found. Breast feeding is still considered the optimal feeding and is particularly emphasized.

Nutritional disturbance is held to be a functional alteration resulting in anatomopathologic disturbances, the three fundamental factors back of which are predisposition to infection, diarrhea and edema.

The newborn infant is poor at antibody formation owing to dependence on the mother. These defenses gradually develop in the baby who is well and naturally fed.

SCHLUTZ, Chicago.

CALCIUM BALANCE IN INFANCY. J. E. CELORIA, Rev. Soc. de pediat. de Rosario **2**:242 (Oct.) 1937.

Twenty-two determinations of calcium balance on infants with an exudative diathesis indicated no appreciable difference from the calcium balance of normal infants. The author is of the opinion that calcium is not a factor in the condition.

SANFORD, Chicago.

INFLUENCE OF PHOSPHORIC ACID ON MINERAL METABOLISM. E. BAUER, Monatschr. f. Kinderh. **71**:374 (Dec.) 1937.

Five children aged from 5 to 12 years received daily 100 cc. of a 1 per cent solution of phosphoric acid for a period of six weeks, in addition to their regular diet. Their blood serum was studied for its content of calcium, potassium, sodium, chlorine, phosphorus, albumin, nonprotein nitrogen and alkali reserve. No effect could be found. No clinical effect was noted either.

GERSTLEY, Chicago.

INFLUENCE OF ULTRASOUND WAVES ON MILK. K. MICHIO, M. TATSUMI and K. KONISCHI, Ztschr. f. Kinderh. **59**:193 (Oct. 14) 1937.

Ultrasound waves cause considerable destruction of vitamin C in milk (presumably attributable to oxidation by gas bubbles containing oxygen formed in the ultrasound wave field). They also cause homogenization of milk and decrease in the depth of the cream layer.

SIEMSEN, Chicago.

CHANGES IN CARBOHYDRATE METABOLISM AFTER ADMINISTRATION OF FAT. E. HOELLISCHER, Ztschr. f. Kinderh. **59**:257 (Dec. 24) 1937.

With a single exception (in a case of uncontrolled diabetes) experiments on 20 healthy and 4 diabetic children and 2 children on a ketogenic diet yielded no increase or a lowering of blood sugar after an olive oil meal, indicating that the body is unable to produce carbohydrates from fats.

SIEMSEN, Chicago.

VARIATIONS OF THE BLOOD SUGAR CURVE IN INFANTS AFTER EXPOSURE TO SUN. M. J. OLEVSKY and L. L. ZELENKO, J. Ukranian Sc. Inst. Maternal & Child Health, 1937, p. 28.

Observations were made on 8 infants in perfect health, from 7 to 14 months of age, and on 4 young dogs from 3 to 4 months of age. After exposure of the infants to the rays of the sun for forty-five minutes, the blood sugar curve was lower as compared with that of the controls, kept indoors. After irradiation the infants and experimental animals showed an elevation of temperature. The part played by overheating in lowering the sugar curve was established by a series of experiments done on sunny but windy days. There was no lowering of the blood sugar curve under these circumstances.

SEMENENKO-MCKHANN, Boston.

TREATMENT OF FISSURES OF THE NIPPLES BY APPLICATION OF COD LIVER OIL. N. D. CHAPIRO, J. Ukranian Sc. Inst. Maternal & Child Health, 1937, p. 34.

Chapiro reports that 298 patients were treated for fissure of the nipple by application of unsterilized cod liver oil, after which the breast was protected by a thin piece of rubber sheeting. Complete healing was observed in 88 per cent and notable amelioration in 12 per cent of the cases in which the lesion was mild. More severe fissures showed less striking improvement.

SEMENENKO-MCKHANN, Boston.

TREATMENT OF DEHYDRATION IN TOXIC STATES. I. M. BERCOVITCH and E. I. KANTOROVITCH, Pediatriya, 1937, p. 10.

Injections of 20 per cent dextrose solutions made into the longitudinal sinus induce temporary improvement of the circulation and diuresis. A study of the hydration of the blood two and twenty-four hours after the injection of dextrose gives some indication of the movement of water between the tissues and the blood. The level of residual nitrogen in the blood fell after the injection of dextrose in those infants who ultimately recovered, but in those whose condition terminated fatally the fall in residual nitrogen was less constant.

SEMENENKO-MCKHANN, Boston.

INFLUENCE OF THE TECHNIC OF FEEDING ON THE GASTRIC ACIDITY OF INFANTS. T. KOSKI and L. LIUKKONEN, Acta pædiat. **21**:250, 1937.

Briefly, the more rapidly the infants took their formulas the more acid were their gastric contents when these were aspirated two hours after feeding. The phenomenon is explained on the basis of two considerations: (1) the shorter the time of nursing the smaller the quantity of alkaline saliva swallowed; (2) the more rapid the evacuation of the bottle the more rapid the distention of the stomach. The validity of the second point was confirmed by pumping air into the empty stomachs of 2 infants until the viscera were visibly distended and then determining the p_H. Values were found comparable with those obtained in infants who had taken their formulas with extreme rapidity. The same result was *not* realized by irritating the gastric mucosa mechanically with the catheter used in gavage.

The problem was suggested by the fact that one of the children's institutions in Helsingfors, Finland, has long been committed to the policy of using nipples perforated with holes 2 mm. in diameter instead of the usual 0.5 mm. or smaller. From a practical point of view, the large holes have given entire satisfaction.

MCCUNE, New York.

RELATION OF INFANT MORTALITY AND STILLBIRTHS TO THE SEASONAL FLUCTUATIONS OF THE CEVITAMIC ACID CONTENT OF THE BREAST MILK OF FINNISH MOTHERS. E. I. SINKKO, Acta pædiat. **21**:407, 1937.

Sinkko believes that his investigations reveal a relationship between the seasonal fluctuations of the cevitamic acid content of mother's milk and the death rate of infants, including those who are born dead.

MCCUNE, New York.

PRODUCTION OF BREAST MILK IN FINNISH MOTHERS AS JUDGED BY STATISTICS RELATING TO WET NURSES. L. YLINEN, Acta pædiat. **21**:473, 1937.

Like most statistical compilations, this one loses much of its detail in abstracting. The following excerpts indicate its content: The average amount of milk produced daily by 82 wetnurses was 1,195 (probable error of mean) ± 49 Gm.; the mean yield of expressed milk was 732 ± 46 Gm.; the average maximal daily

output was 1,788 ± 69 Gm., and the mean production during the best month of lactation was 47.8± 2.2 Kg. These figures compare favorably with those relating to German wetnurses. In general, the most dependable index of the productivity of a given wetnurse is the amount of milk secreted during the best month of lactation; the peak of productivity is unfailingly reached during the second or third trimester of lactation. The best time to select a wetnurse is when her child is from 4 to 8 weeks old. Generally, the weight of the wetnurse increases in proportion to the amount of breast milk produced; in some cases the two variables are not correlated; in others the correlation is inverse. The productivity of wetnurses under institutional circumstances is in no small measure related to emotional influences.

McCUNE, New York.

Vitamins; Avitaminoses

THE METABOLISM OF PYRUVIC ACID IN VITAMIN B_1 DEFICIENCY AND IN INANITION. M. A. LIPSCHITZ, V. R. POTTER and C. A. ELVEHJEM, J. Biol. Chem. **123**:267, 1938.

The primary biochemical abnormality associated with vitamin B_1 deficiency appears to be a failure of the organism to metabolize pyruvic acid. Lipschitz, Potter and Elvehjem measured the oxygen uptake of homogenized tissue with and without added pyruvate, as well as the removal of the pyruvate by the liver, kidneys and brain of normal, fasting and polyneuritic chicks. It was shown that the ability of the kidneys, liver and brain to utilize pyruvate as a substrate is impaired in animals with polyneuritis. The derangement is greatest in the brain. The liver and kidney of fasting birds show decreased ability to remove added pyruvate. The brain does not show this effect of fasting. Removal of pyruvates by the liver and kidney in fasting birds approximates that found in birds with polyneuritis. Oral administration of dextrose to fasting birds resulted in restoration of the ability of the liver to remove pyruvate. Similar feeding of dextrose to birds with polyneuritis resulted in deposition of liver glycogen and increased ability to remove pyruvate, though normal values were not reached. The failure in the case of polyneuritic birds to obtain complete restoration of the ability to remove pyruvate when dextrose was fed shows that inanition is not the sole explanation of the derangement of pyruvate metabolism, although it is a complicating factor.

PAGE, Indianapolis. [ARCH. NEUROL. & PSYCHIAT.]

ASYMPTOMATIC SCURVY: ITS RELATION TO WOUND HEALING AND ITS INCIDENCE IN PATIENTS WITH PEPTIC ULCER. T. H. INGALLS and H. A. WARREN, New England J. Med. **217**:443 (Sept. 9) 1937.

In this article Ingalls and Warren present a series of 20 cases of peptic ulcer, with studies of the level of vitamin C in the blood plasma of the patients.

One of the authors had previously pointed out that saturation "is a state so far removed from scurvy that urinary tests become of questionable value as a purely diagnostic procedure." He found the determination of the plasma to be the best single index of vitamin C nutrition in an infant.

Of the 20 patients with gastric or duodenal ulcers 18, or 90 per cent, were found to have low values, 12 of whom had values of 0.2 mg. of vitamin C per hundred cubic centimeters or less as compared with the normal range of from 0.6 to 2 mg. In most of these cases it could be demonstrated that the patients had taken an inadequate amount of vitamin C, and there is evidence that if a sufficient amount of the vitamin is ingested the blood values can be raised to normal. The theoretic importance of these findings in relation to the healing of peptic ulcer, to the bleeding of the ulcer and to surgical intervention is discussed.

GENGENBACH, Denver.

THE FUNDUS OCULI OF THE RABBIT WITH VITAMIN A DEFICIENCY. F. SCULLICA and E. FULCHIGNONI, Ann. di ottal. e clin. ocul. **65**:427 (June) 1937.

Spotted or brown rabbits were placed on a diet deficient in vitamin A. The fundi were observed after dark adaptation of thirty minutes and after exposure of one eye to a light of 500 foot candles for four hours. The fundus of the exposed eye was compared with that of the unexposed eye at various intervals after exposure and with that of a rabbit on a normal diet and treated to the same exposure. In animals on a diet deficient in vitamin A, as well as in those on a normal diet, a definite decoloration of the fundus was observed in the eye exposed to light. This decoloration was attributed to bleaching of the visual purple. In animals on a normal diet the color returned to normal in from seventeen to eighteen hours after exposure, while in those on the deficient diet the difference in color persisted much longer, the length of time required for a return to the normal color being proportional to the severity of the deficiency in vitamin A.

In addition to this decoloration, there was seen in normal animals and more markedly in animals with vitamin deficiency a change in pigmentation of the fundus after exposure to light. The homogeneous pigmentation of certain areas was replaced by smaller zones of pigment-forming islands and archipelagos of pigment surrounded by clear areas in which the choroidal vessels were clearly seen. The phenomenon was reversible after dark adaptation but became less so in animals with more severe vitamin deficiency. Another phenomenon observed was the appearance of medullated nerve fibers, which extended from the disk to the periphery in all directions after exposure to light. After dark adaptation, this picture was replaced by the normal one, showing the medullated nerve sheaths only near the optic disk. The changes described were all seen at a time before the symptoms of xerosis and keratomalacia occurred.

GIFFORD, Chicago. [ARCH. OPHTH.]

EFFECT OF DEXTROSE ON THE VITAMIN C CONTENT OF THE LIVER AND OF THE ADRENAL GLANDS. J. GAGYI, Lattante **8**:459 (Aug.) 1937.

In guinea pigs on a scurvy-producing diet the giving of pure 10 per cent dextrose caused an increase of vitamin C in the adrenal glands and liver.

HIGGINS, Boston.

STUDIES ON VITAMIN C. R. B. ENCINA, Arch. hosp. de niños **7**:119 (Sept.) 1937.

Encina reports a study of 60 infants suspected of having scurvy; of these, 19 had latent and 2 had genuine scurvy. He used Tillman's method in making the diagnosis. He offers the following conclusions: Deficiency occurs with values below 9 mg. of vitamin C per hundred cubic centimeters of blood. The amount of vitamin C in the urine varies with the amount ingested and with the concentration in the blood. More than 15 mg. of vitamin C in the urine shows the tissues to be saturated. Tissues deficient in vitamin C can be saturated in six days if proper doses are used. Parenteral administration hastens improvement. There are no contraindications even to large doses (400 mg.). Oral administration may be less effective because of infections or because of changes in the intestines which may be caused by the vitamin deficiency.

Human milk contains from 20 to 50 mg. of the acid per liter; cow's milk, 10 mg. From 25 to 50 cc. of orange juice contains from 15 to 30 mg. About 15 to 30 mg. should be given daily to infants who do not get sufficient breast milk or are artificially fed. More is needed by congenitally weak infants, premature infants, twins and children of parents suffering from alcoholism. More should be given in winter if the infant is fed cow's milk. Capillary alterations are not proportional to the amount of cevitamic acid in the blood. About 50 per cent of the subjects had the Rumpel-Leed sign.

SCHLUTZ, Chicago.

THE BONE MARROW OF PATIENTS WITH RICKETS. P. LIESSENS, Monatschr. f. Kinderh. **72**:22 (Jan.) 1938.

This is the second of a series of studies in which Liessens examined bone marrow obtained from the living infant by puncture of the tibia. In 12 cases of rickets he found no demonstrable change.

GERSTLEY, Chicago.

CAMPAIGN AGAINST RICKETS. DE RUDDER, München. med. Wchnschr. **84**:1841 (Nov. 19) 1937.

Rudder calls attention to the surprising prevalence of rickets. Seventy per cent of the infants between 4 and 12 months of age who were admitted to the Children's Hospital of Frankfort on the Main, Germany, for various conditions were found to have florid rickets. The same observation is being made in other parts of Germany. The extensive bony deformities which were prevalent in the past are less frequent now. However, changes in the bony pelvis, which become obvious in later years, are a danger in childbirth. Rickets increases the mortality of infants indirectly. The mortality rate from bronchopneumonia is six times greater among rachitic children than among those without rickets. The prevention of rickets has not been given enough attention by the physicians in welfare clinics. For ten years there have been methods for the prevention and cure of rickets. It is important to remember that rickets is likely to develop in premature infants and twins and that the winter months predispose to this disease. The author stresses some important clinical symptoms. He gives a table of the prophylactic and therapeutic doses of vitamin D concentrate and cod liver oil.

BRAHDY, Mount Vernon, N. Y.

ASCORBIC ACID CONTENT OF MANCHURIAN PAPRIKA. M. SUGIURA, J. Orient. Med. **28**:175 (Feb.) 1938.

Of Manchurian paprikas, capsicum annum L. var. acuminatum Fingerth was found to be richest in ascorbic acid, capsicum annum L. var. cerasiforme Irish being the next richest and capsicum annum L. var. grossum Sendt the poorest. Even in the same variety of paprika the quantity of ascorbic acid differs according to the soil in which the plants were grown. The extract of the acid is not destroyed if distilled and condensed in vacuum at from 30 to 35 C. Likewise no changes are observed when the extract is dried with lactose or with sulfuric acid as a desiccator and stored in a vacuum. When the extract was stored under exposure to air, 54.77 per cent was lost within twenty days; if the container was corked, the loss was 13.02 per cent.

KATO, Chicago.

DYSADAPTATION IN CHILDREN. K. U. TOVERUD, Acta pædiat. **20**:225, 1937.

Toverud examined 399 children with reference to their capacity for visual adaptation in the dark by his modification of the test which was originally devised by Edmund. One half of the group represented comparatively poor hygienic surroundings, and the other half, relatively better economic circumstances. The first examination was made in November 1935. Of the poorer children, only 33 per cent showed normal ability to adapt to darkness, whereas 72 per cent of the more fortunately endowed children gave a normal response. Smaller but representative portions of the two groups were tested a second time at the end of March 1936, after seven months in school. At this examination less difference was noted in the average responses of the two groups: Normal ability was demonstrated in 37 per cent of the poor children and in only 47 per cent of their more fortunate fellows. A third examination was carried out in August 1936. Marked improvement was recorded; 62 per cent of the first group and 81 per cent of the second showed normal adaptation to darkness. Inquiry revealed a positive and fairly reliable correlation between the capacity of the subjects to adapt to darkness and the amount of vitamin A which they ingested.

MCCUNE, New York.

SOME CASES OF SCURVY. L. J. RENDERS, Nederl. tijdschr. v. geneesk. **82**:1069 (March 5) 1938.

After a brief review of the various cutaneous manifestations that may occur in scurvy, Renders describes 6 patients whom he has observed in the course of two years. Among these were 3 young men of unemployed families, who lived with their families and therefore were not able to exercise any care in the composition of their meals. In the author's opinion, keratosis suprafollicularis has no value for the diagnosis of incipient scurvy. One of the patients presented a scleroderma-like change of the skin of the legs such as was described for scurvy by Morawitz and Pfeiffer.

VAN CREVELD, Amsterdam, Netherlands.

Hygiene; Growth and Nutrition; Public Health

PROVISIONAL BIRTH, DEATH AND INFANT MORTALITY RATES FOR 1937. Pub. Health Rep. **53**:1072 (July 1) 1938.

According to the provisional nation-wide tabulations of the United States Bureau of Census, the infant (under the age of 1 year) mortality rate per thousand live born infants for the United States in 1937 was 54.4. This is the lowest in the history of the bureau. Tables are given, showing the death and the birth rate for each state. The lowest birth rate was in New Jersey, with 12.6, but this state had the lowest infant mortality rate, 39.4. New Mexico had both the highest birth rate and the highest infant mortality rate.

SANFORD, Chicago.

INFLUENCE OF METHODIC EXERCISES IN THE DEVELOPMENT OF THE HEALTHY SUCKLING. M. H. BORTAGORAY, An. Soc. de puericultura de Buenos Aires **3**: 11 (Jan.-March) 1937.

The author comments on the value of routine exercises of the arms, legs and trunk of the suckling and mentions a few of the exercises used.

HERRON, Monroe, La.

CENTRALIZATION OF MILK KITCHENS IN THE PROTECTION OF EARLY INFANCY. J. R. ABDALA, J. C. PELLERANO and J. S. SALABERRY, An. Soc. de puericultura de Buenos Aires **3**:14 (Jan.-March) 1937.

The authors consider the advantages of having a milk kitchen in connection with a central dispensary for the proper preparation and sterilization of artificial formulas. This is especially advantageous in the poorer communities, where hygiene is not prevalent and where special formulas are necessary for the various types of malnutrition and digestive upsets. The mothers cannot prepare many formulas correctly; also, there should be variation of formulas, with uniformity of preparation and without contamination. In the milk kitchen which the authors cite as an example there is a personnel of 28 carrying out the various functions of the kitchen.

HERRON, Monroe, La.

THE MILK KITCHEN—ITS ORGANIZATION AND FUNCTION. J. BAYLEY BUSTAMANTE, An. Soc. de puericultura de Buenos Aires **3**:19 (Jan.-March) 1937.

The author describes in detail the departmental organization of a milk kitchen, the functions of the personnel and the financing of such a proposition.

HERRON, Monroe, La.

A CONTRIBUTION ON INFANT MORTALITY IN BRAZIL. C. MARQUES DIAS, Arch. de pediat., Rio de Janeiro **10**:497 (July) 1938.

The author concludes that infant mortality in Brazil is higher than it should be. The greatest causes of death are diarrhea and enteritis. These conditions are

due to errors of feeding, and their incidence might be reduced by better supervision of the mothers and infants and by furnishing breast milk to artificially fed babies who are in poor condition.

SANFORD, Chicago.

THE INSTITUTE OF PUERICULTURE, RIO DE JANEIRO. M. GESTEIRA, Bol. Inst. de puericultura, Rio de Janeiro **1**:19, 1938.

The Institute of Puericulture was created in 1937 to study and advance the life of the child. This is accomplished by research work and education. Education will be given to three groups: young girls, "society ladies" and medical students and physicians. The model installation of these services should conform strictly with the requirements of modern science. Interesting pictures are shown of the plans and model of the institute.

SANFORD, Chicago.

SOME COMMENTARIES ON ESTAPÉ'S REPORT OF A NIPIOLOGIC SCALE. M. GESTEIRA, Bol. Inst. de puericultura, Rio de Janeiro **1**:33, 1938.

Estapé's scale was reported in the *Revista médica latino-americana*. Gesteira proposes to modify the scale by introducing a seventh series, the genetic series, in connection with the values of the constitution which should be considered the basis, and the addition at each series of a plus 1 value to designate the superlative degree, the value above the normal, which is frequently found in practice for each of the aspects of development. For the six series one might form a hexagonal pyramid the base of which should be the genetic series, sustained by the four mainstays which Langstein and Meyer consider rightly the fundamentals in the formation of the phenotype.

SANFORD, Chicago.

DEMOGRAPHIC EVOLUTION AND INFANT MORTALITY. J. DE CASTRO, Bol. Inst. de puericultura, Rio de Janeiro **1**:125, 1938.

According to the relations between the incidence of birth and that of death, there is a demographic curve in each country that is peculiar to its economic type. In some there are a low birth and a low mortality rate; in others, a high birth and a high mortality rate. Brazil is a country where infant mortality is very high, and the reduction of the incidence of death in infants should be national problem no. 1.

SANFORD, Chicago.

INFANT MORTALITY IN FINLAND FROM 1750 TO 1935. P. HEINIÖ, Acta pædiat. **21**:166, 1937.

The precise details of this communication are of greater national than international interest. Since 1750, when the keeping of vital statistics was commenced, infant mortality has fallen from 28.48 per hundred liveborn infants per annum to 7.36. The number of deaths during the neonatal period has diminished remarkably. During the same period the birth rate has fallen from 45.3 per thousand living inhabitants per annum to 18.4. The cities have led in the betterment of mortality. Although vastly lower than in former times, the death rate of illegitimate infants is still higher than that of infants born in wedlock.

MCCUNE, New York.

STUDIES OF SO-CALLED UNDERWEIGHT SCHOOL CHILDREN. A. RUOTSALAINEN, Acta pædiat. **21**:308, 1937.

The simple ratio between weight and height at different ages is not an adequate index of the state of the child's nutrition; underweight is not necessarily the equivalent of undernutrition. In addition to purely dimensional factors, the type of body build, the color of the skin and mucous membranes and the state of development of the subcutaneous tissue and of the skeletal musculature must all be kept in mind in judging the physical status of the child.

MCCUNE, New York.

Prematurity and Congenital Deformities

A Premature Infant Weighing Seven Hundred and Thirty-Five Grams and Surviving. S. J. Hoffman, J. P. Greenhill and E. C. Lundeen, J. A. M. A. **110**:283 (Jan. 22) 1938.

The authors mention previous reports of premature infants weighing less than 1,000 Gm. who have lived and describe the care of one weighing 735 Gm. at birth, whose weight dropped to 595 Gm. on the eighth day. This child grew up to become a normal though small child.

H. S. Heersma, Kalamazoo, Mich.

Congenital Deformity of the Upper and Lower Extremities. L. Bocchi, Lattante **8**:618 (Nov.) 1937.

This article reviews the various congenital deformities of the extremities and outlines in brief the correct orthopedic treatment for each.

Higgins, Boston.

Death from a Syndrome, "Pallor and Hyperthermia," in Young Twins. M. Zampetti, Pediatria **45**:345 (April) 1937.

Zampetti illustrates a rare incident which happened in the hospital of Pontremoli, Italy. Twins died on the same day and at an equal interval of time after operation for right inguinoscrotal hernia causing a syndrome of "pallor and hyperthermia."

He has not been able to find any literature describing such an incident in which death came so rapidly and in which there was this syndrome accompanied by convulsions. He believes that etiologically this strange syndrome is to be attributed to a congenital imbalance of endocrine function.

Palmieri, Brooklyn.

Four Cases of Abdominal Fissure, Scoliosis, Eventration and Absolute Lack of Anomalies of the Inferior Extremities. G. Ilberg, Ztschr. f. Geburtsh. u. Gynäk. **115**:463 (Sept.) 1937.

This article gives a description of these cases and a review of similar cases in the medical literature.

Adair and Landé, Chicago.

Total Hemihypertrophy and Hemiatrophy: The Unusual Case of an Infant, Complicated by Spontaneous Gangrene of an Extremity. H. L. Kottmeier, Acta pædiat. **20**:530, 1938.

An infant born by breech presentation exhibited shortly after delivery extensive gangrene of the right hand; this was apparently not due to vascular damage or to infection, although the right humerus had been broken in the process of extraction. A little while later it became apparent that the child, a boy, was affected by total hemihypertrophy of the left side of the body; the bones were affected as well as the soft parts. The asymmetry was progressive during the first year of life, the period covered by the reported observation. Roentgen examination revealed small calcified masses in the regions of both adrenal glands. The concentration of the blood chloride was not diminished.

Gangrene of the extremities in infants is occasionally seen as the result of amniotic adhesions, sepsis, syphilis, scarlet fever and measles; "spontaneous" gangrene is extremely rare. The prognosis is poor, irrespective of the cause.

Kottmeier discusses the reported cases of hemihypertrophy and hemiatrophy, emphasizing the unproved character of the various hypotheses that relate to their causes. Genetic disturbances afford a plausible explanation of hemihypertrophy in some of the cases and inflammatory disease of the central nervous system appears to be responsible for hemiatrophy in many of the cases. The bibliography is of unusual value.

McCune, New York.

MORTALITY OF PREMATURELY BORN INFANTS IN THE UNIVERSITY PEDIATRIC CLINIC OF HELSINGFORS DURING THE YEARS FROM 1916 TO 1936. I. KIJANEN, Acta pædiat. **21**:224, 1937.

Because of the decline of the death rate of infants under 1 year of age in nearly all civilized countries during the last two decades, the mortality of premature infants now constitutes a considerable fraction of the first year death rate. Much progress had been made in procuring the survival of prematurely born infants. At the present time their deaths are due principally to congenital debility, injuries sustained at birth and pneumonia. Statistics relating to observations at Ylppö's clinic are presented in graph and table.

McCUNE, New York.

Newborn

PNEUMONIA IN NEWBORN AND STILLBORN INFANTS. M. WARWICK, New York State J. Med. **37**:2075 (Dec. 15) 1937.

On gross examination pneumonia in the newborn resembles areas of hemorrhage and atelectasis. For this reason microscopic sections should always be examined. Warwick reports, from the Millard Fillmore Hospital, Buffalo, 500 consecutive autopsies on infants who were stillborn or died in the first ten days of life. More than one fifth of these showed a pneumonic process in the lung. Seventy-one per cent of those showing pneumonia revealed no bacteria in the lung. She believes that the pneumonia was caused by aspiration of toxic bile salts and cornified epithelial cells from the amniotic fluid. In most of these cases there was a history of long and complicated labor. AIKMAN, Rochester, N. Y.

RESPONSE OF THE NEWBORN TO RESTRAINT. F. STIRNIMANN, Rev. franç. de pédiat. **13**:496, 1937.

Gloves tied about the hands of the newborn infant evoke the movements of rubbing the hands and arms against each other, with eventual removal of the gloves by this means. The reaction seems to be instinctive and is lost after twenty-three days. The older infant (aged from 2 to 3 months) uses a different method of getting rid of the gloves, pulling them off with his hands.

LESLIE, Evanston, Ill.

RECENT CASES OF FAMILIAL ICTERUS GRAVIS IN THE NEWBORN. M. PÉHU, R. NOEL and A. BROCHIER, Rev. franç. de pédiat. **13**:565, 1937.

The histories of 70 cases of icterus gravis of the newborn are presented. Of these cases, 5 came under the personal observation of the authors. In so large a series the familial incidence is even more striking than it is in isolated cases, although the authors give little consideration to the mode of inheritance. It is interesting to note that clinically icterus gravis in association with erythroblastosis and erythroblastemia cannot be differentiated from icterus gravis not associated with such changes in the peripheral blood or bone marrow. This leads Péhu and his collaborators to the opinion that the appearance of large numbers of nucleated red cells is a secondary rather than a primary feature of this condition. In treating the condition, in addition to blood transfusions in the newborn in which the icterus appears, the authors advocate the administration of liver extract in large quantities to the mother during pregnancy.

LESLIE, Evanston, Ill.

BIOMETRIC DATA ON NEWBORN INFANTS IN TURIN, ITALY. R. SIMONETTI CUIZZA, Lattante **8**:469 (Aug.) 1937.

Biometric data on 4,000 newborn infants of Turin are listed. The mean weight of the boys was 3.27 Kg.; that of the girls 3.11; that of the newborn offspring of

primiparous mothers, 3.1 Kg., and that of the newborn offspring of multiparous mothers, 3.2 Kg. The mean height was 49.7 cm. for boys and 48.75 for girls. The mean circumference of the head was 34.14 cm. for boys and 33.66 for girls. The mean circumference of the chest was 32 cm. for boys and 31.17 for girls. Tables are given listing the average sizes of newborn infants as reported from different parts of Italy.

HIGGINS, Boston.

SUBCUTANEOUS GUMMA IN A NEWBORN INFANT. J. C. C. BORDON, Arch. de pediat. d. Uruguay **8**:763 (Dec.) 1937.

A subcutaneous gummatous lesion is described in an infant 28 days old. He showed signs of congenital debility, and there were syphilitic manifestations in the parents. Spirochetes were found in the lesions of the child's lips and in the tissue obtained for biopsy. The infant rapidly declined and died twelve days after he was first seen.

SCHLUTZ, Chicago.

ANAEMIA NEONATORUM. H. LEHNDORFF, Ergebn. d. inn. Med. u. Kinderh. **52**: 611, 1937.

Lehndorff defines anaemia neonatorum as a deficiency of blood which in most cases sets in suddenly at the end of the first week of life. It develops in a previously healthy infant born to healthy parents. It is a monosymptomatic affection, i. e., aside from pallor, there is no other phenomenon of disease. Another characteristic is a striking tendency toward spontaneous and definite cure. Study of the blood yields the picture of hyperchromic anemia, the color index being high, without, however, marked alteration of the red blood corpuscles. Finally, the author stresses the negative element, namely, the absence of any evident etiologic factor. Because of the sudden, almost explosive onset, the condition was at first thought to be due to maternal toxins incident to pregnancy, but in all cases the mother was found to be healthy. If evidence of an acute infection in the infant were demonstrable, the anemia would be classified as acute febrile hemolytic anemia of the Lederer type, but in none of the cases was infection demonstrated. The author therefore concludes that although anaemia neonatorum is clinically and hematologically a well defined disease, physicians still are ignorant of its causative factors; however, he seems to feel that the anemia may be a result of some reaction of pregnancy or an allergic manifestation.

CAPPER, Philadelphia.

A POSTMORTEM STUDY OF THE EFFECTS OF BIRTH ON THE CENTRAL NERVOUS SYSTEM OF THE NEWBORN. F. HAUSBRANDT and A. MEIER, Frankfurt. Ztschr. f. Path. **49**:21, 1936.

The brains and the spinal cords of 103 of 138 infants who died shortly before or following delivery were examined. Tears in the tentorium cerebelli were three times as frequent in full term infants and intraventricular hemorrhages twice as frequent in the premature ones.

Damage of the spinal cord, usually present in the cervical region, was noted in 23 per cent of the cases. The authors stress the importance of examining the spinal cord in all cases in which examination of the remainder of the body fails to disclose the cause of the death.

OHRINGER. [ARCH. PATH.]

TETANY OF THE NEWBORN. H. BAAR, Monatschr. f. Kinderh. **71**:321 (Dec.) 1937.

This article includes an extensive review of the literature. From this review and from 2 cases reported Baar concludes that the subject of tetany in the newborn is not as simple as some believe. He admits that there may be cases in which tetany is on a rachitic basis. But in many of the reported cases this observation has not been confirmed by chemical studies of the blood and determinations

of electrical irritability. Unquestionably occasional cases reported as instances of tetany may be instances of tetanus neonatorum or of acute encephalitis. Many, of course, are instances of brain hemorrhage. To this group Baar adds two other clinical entities in which the clinical picture was that of tetany while all tests ruled out the possibility of rickets. One of these conditions was associated with an unusually high level of the blood phosphorus. While blood calcium remained between 10 and 11 mg. per hundred cubic centimeters, blood phosphorus remained constant between 7.8 and 8.6 mg. The second condition was due to alkalosis following hyperventilation, the excessive breathing being due presumably to an enlarged thyroid pressing on the trachea.

GERSTLEY, Chicago.

INSIDIOUS UMBILICAL INFECTION IN INFANTS. E. CALDERÓN, München. med. Wchnschr. **85**:1226 (Aug. 12) 1937.

Calderón reports an unusual case in which a necropsy was made. It concerns an apparently well newly born infant who was given lemon juice milk because it was considered a "lazy breast feeder." The separation of the umbilical cord had been uneventful. At 6 weeks of age the infant was admitted to the hospital with a temperature of 39.5 C. (103.1 F.) and abdominal distention and tenderness. A small umbilical hernia which had been present in the first weeks was now more prominent. During the next few days there were vomiting, diarrhea and an increase in abdominal distention. Incision revealed considerable thin pus in the abdomen. The child died four days after operation.

Autopsy disclosed thin purulent fluid in the abdomen, increased inflammation around the umbilical artery, numerous small abscesses in the liver, and an inflammatory reaction of the adventitia of the umbilical vein. The umbilical artery was not affected.

Apparently the infection had traveled up the umbilical vein without a reaction at its original site—the umbilicus—but with a reaction and abscess formation in the liver.

BRAHDY, Mount Vernon, N. Y.

OCCURRENCE OF MELAENA NEONATORUM IN FINLAND AND ITS RELATIONSHIP TO CERTAIN INFECTIOUS DISEASES. A. KEPILÄ and E. LEPPO, Acta pædiat. **21**: 208, 1937.

On the basis of a statistical survey of 177 cases of melena in newly born infants it is demonstrated that the incidence of the manifestation showed a certain seasonal periodicity; this periodic character was correlated in a positive sense with the occurrence of the common infectious diseases.

MCCUNE, New York.

TREATMENT OF WHITE ASPHYXIA IN THE NEWBORN. N. J. F. POMPE VAN MEERDERVOORT, Nederl. tijdschr. v. geneesk. **81**:5795 (Dec. 4) 1937.

In the treatment of asphyxia neonatorum, especially if the heart action is poor, coramine (a 25 per cent solution of pyridine betacarbonic acid diethylamide) should not be injected subcutaneously but into the umbilical vein. The author describes 2 examples of this form of therapy.

VAN CREVELD, Amsterdam, Netherlands.

Acute Contagious Diseases

PROTECTIVE ACTION OF SULFANILAMIDE AND ANTIMENINGOCOCCUS SERUM ON MENINGOCOCCUS INFECTION OF MICE. T. MCPHERSON BROWN, Bull. Johns Hopkins Hosp. **61**:272 (Oct.) 1937.

In protective influence, 8 mg. of sulfanilamide is comparable with 0.1 cc. of a highly potent antimeningococcus serum.

The combination of sulfanilamide and antimeningococcus serum produces a greater degree of protection than either of the agents by itself. In a few animals the use of antipneumococcus serum instead of antimeningococcus serum in combined therapy failed to give enhanced protection.

The percentage of positive blood cultures, taken eight hours after the mice were infected, was lower for the group of mice treated with the combination of sulfanilamide and antimeningococcus serum than for the groups treated with these therapeutic agents individually. FROM THE AUTHOR'S SUMMARY.

FUNDAMENTALS OF SERUM THERAPY. W. H. TUCKER, Illinois M. J. **72**:494 (Dec.) 1937.

Certain serum preparations are distributed to physicians of Illinois by the state department of public health. In this review Tucker summarizes the state department's experiences and opinions.

Diphtheria immunization has been carried out on a wide scale in Illinois, but there are many thousands of children still unprotected. The use of antitoxin for Streptococcus scarlatinae as a prophylactic measure is not recommended by the state department. The antitoxin is of value in treating severe scarlet fever. The limited supply of human convalescent serum for treating scarlet fever renders it unlikely that this product can be employed on a wide scale. The intravenous route is preferable to the intraspinal one for the injection of meningococcus antiserum or antitoxins. Pneumococcus antiserum is not employed on a scale commensurate with its value. Tetanus antitoxin is used almost entirely for prophylactic purposes. An effective polyvalent antiserum for treating dysentery is available. A polyvalent serum is available which has been used effectively in the treatment of certain snake bites.

The state department of public health has employed human convalescent serum in treating poliomyelitis during the past five years with satisfactory results. This product should be used in much larger amounts than were employed in New York in 1931. In Tucker's opinion, the use of convalescent serum should be continued until a more effective therapeutic agent is made available for the treatment of poliomyelitis. Human convalescent serums have been used in treating chickenpox, measles and mumps but not yet on a large scale.

Serum reactions are becoming less frequent since procedures for the refinement and concentration of serum products have been applied. In the department's experience, delayed serum sickness has occurred in as high as 50 per cent of persons to whom a preparation of animal serum has been administered. Previous desensitization does not prevent the development of delayed serum sickness.

BARBOUR, Peoria, Ill.

THE USE OF POOLED HUMAN CONVALESCENT SCARLET FEVER SERUM IN SURGICAL STREPTOCOCCIC INFECTIONS. S. L. GOLDBERG, Illinois M. J. **72**:500 (Dec.) 1937.

Twenty-eight cases are reported, in which septic surgical streptococcic infections were treated with pooled human convalescent serum. The mortality was 15 per cent. Goldberg believes that serum therapy was of definite value in this group of cases.

BARBOUR, Peoria, Ill.

HUMAN CONVALESCENT SERUM AND ITS APPLICATION TO ACUTE INFECTIOUS DISEASES. S. O. LEVINSON, E. PENRUDDOCKE and A. M. WOLF, Illinois M. J. **72**:514 (Dec.) 1937.

The activities and experiences of the Samuel Deutsch Serum Center in Chicago are reviewed. Rigorous care of the preparation, and attention to the handling, of the human convalescent serum to insure a potent and safe product are stressed. Scarlet fever convalescent serum has been found effective in both prophylaxis and therapy. Measles convalescent serum has proved to be a valuable prophylactic

agent. The treatment of patients with poliomyelitis by injections of convalescent serum has resulted in less than 2 per cent paralysis in over 200 consecutive cases. Early diagnosis and early intravenous administration of serum in massive doses are important. Levinson urges that studies of this form of therapy be continued.

BARBOUR, Peoria, Ill.

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ELEMENTARY BODIES OF VACCINIA FROM INFECTED CHORIOALLANTOIC MEMBRANES OF DEVELOPING CHICK EMBRYOS. J. E. SMADEL and M. J. WALL, J. Exper. Med. **66**:325, 1937.

By a method of differential centrifugation and tryptic digestion suspensions of elementary bodies have been prepared from chorioallantoic membranes of chick embryos infected with vaccine virus. The infective titer of the final suspension of elementary bodies was usually the same as that of the original emulsion of tissue. Elementary bodies from infected chick membranes were agglutinated by anti-vaccinal serum obtained from different mammalian species as well as were bodies prepared from inoculated rabbit skin. Seitz filtrates of infected chick material contained soluble precipitable substances of vaccinia; these filtrates and filtrates from infected rabbit skin reacted equally well with rabbit serum which contained either L or S antibodies

FROM AUTHORS' SUMMARY. [ARCH. PATH.]

ANTIMENINGOCOCCIC VACCINATION. N. SILVERTHORNE, J. Immunol. **33**:51, 1937.

Silverthorne presents a modification of the technic for testing the bactericidal power of blood. Guinea pigs inoculated with a phenol-killed vaccine of meningococci resisted a subsequent inoculation with live meningococci. Their blood had no bactericidal properties before vaccination but had a marked titer of bactericidal activity after vaccination. Bactericidal power was also noted in the blood of the few control animals which did not succumb to the injection of live bacteria. Vaccination of 4 children from 10 months to 3 years of age who were without bactericidal properties in their blood was followed by the development of such properties. The action of the blood was specific against the type of meningococci used for vaccination.

DAVIDSOHN, [ARCH. PATH.]

SULPHANILAMIDE IN THE TREATMENT OF ERYSIPELAS. W. R. SNODGRASS and T. ANDERSON, Brit. M. J. **2**:1156 (Dec. 11) 1937.

Two hundred and seventy patients with erysipelas were treated in two groups under controlled conditions with (*a*) ultraviolet rays and (*b*) sulfanilamide. There was an even distribution in the treatment groups in respect to factors known to influence the course of the disease, such as (*a*) the duration of the disease before admission to the hospital, (*b*) the age of the patient, (*c*) the severity of the infection and (*d*) associated diseases.

The average total dose of sulfanilamide was 41.6 Gm., given in fourteen and four-tenths days. The drug was administered in 1, 2 or 3 Gm. doses every four hours until the cessation of primary pyrexia, with an average dose per case of 14.64 Gm.; thereafter 0.75 Gm. was given thrice daily until the patient was dismissed.

Cyanosis occurred in 29.6 per cent of the cases; it was more frequent when the larger doses of sulfanilamide were given.

Sulfanilamide is of benefit in securing curtailment of (*a*) the spread of the lesion, (*b*) the duration of the primary pyrexia and (*c*) the duration of the toxemia. Sulfanilamide reduced the incidence of complications and diminished the tendency to recurrence.

An effective method of treatment is to give 1 Gm. of sulfanilamide by mouth at four hour intervals until the cessation of primary pyrexia, and thereafter 0.75 Gm. by mouth thrice daily until final cure is determined.

ROYSTER, University, Va.

MORPHOLOGIC STUDIES ON VACCINIA VIRUS CULTIVATED IN THE DEVELOPING EGG. F. F. TANG and H. WEI, J. Path. & Bact. **45**:317, 1937.

Examination of the virus of vaccinia cultivated in the chorioallantoic membrane of the chick embryo revealed two types of cytoplasmic inclusion, a large and a small type. The large form appears early in development and may be regarded as a sort of colony in which the small inclusions lodge. Many cells contain only the small bodies, which may appear as diplococcoids, short chains or bacillary structures. In all probability the large form corresponds to the classic Guarnieri body and the small to the Paschen body. These structures have been seen in the living membrane by transmitted light, with or without a supravital stain, by dark field illumination and in stained smears. Dark field examination was not satisfactory on account of the thickness of the membrane. Two possible developmental cycles of the virus are suggested, and the changes in virulence during egg propagation of the virus are discussed. FROM AUTHORS' SUMMARY. [ARCH. PATH.]

VIRULENCE OF CEREBROSPINAL FLUID IN THE COURSE OF SIMPLE MUMPS. V. DE LAVERGNE, P. KISSEL and H. ACCOYER, Bull. et mém. Soc. méd. d. hôp. de Paris **53**:1276 (Nov. 15) 1937.

Lavergne and his collaborators inoculated 8 rabbits suboccipitally with 1 cc. of cerebrospinal fluid from 8 patients suffering from simple parotitis. The changes in the cerebrospinal fluid of the rabbits were observed by punctures at intervals of four days for three or five weeks. At the end of the experiment, microscopic studies of the brains were made. Seven rabbits reacted with persistent hypercytosis (hyperlymphocytosis) during the first ten days. The reaction diminished in the course of the experiment and showed a late recrudescence in 5 animals. The brains of the 5 rabbits that had early and late hypercytotic reactions showed microscopic changes characteristic of neuraxitis and, in 2 cases, also of parotitic radiculitis. The brains of the 2 rabbits that had early, but not late, hypercytotic reaction showed inflammation but no anatomic changes. In the rabbit in which the cytologic reaction of the cerebrospinal fluid was normal meningitis did not develop. The authors conclude that the cerebrospinal fluid of patients who are suffering from simple parotitis is virulent for rabbits in almost all cases. The cerebrospinal fluid is virulent, although the patients do not show clinical symptoms of meningitis and the fluid does not show important cytochemical alterations. Absence of meningitis complicating parotitis in man does not indicate absence of the virus of parotitis in the brain. Development of meningitis in association with mumps does not show an abnormal location of the virus of parotitis, which is present in the cerebrospinal fluid in the course of simple parotitis in all cases. The development of clinical meningitis is probably due to an unknown cause which is independent of the presence or absence in the cerebrospinal fluid of the virus of parotitis. EDITOR'S ABSTRACT. [ARCH. NEUROL. & PSYCHIAT.]

MEASLES PROPHYLAXIS IN CHILDREN'S HOSPITALS. C. PELFORT, Arch. de pediat. d. Uruguay **8**:739 (Dec.) 1937.

The inconvenience of epidemics of measles in children's hospitals is cited. The various prophylactic measures are reviewed. The difficulties of obtaining convalescent serum are stated. As an alternative, Pelfort recommends the use of serum from patients who have had measles and describes the method of collection.

SCHLUTZ, Chicago.

MALIGNANT DIPHTHERIA. M. FABRES, Rev. chilena de pediat. **8**:655 (Nov.) 1937.

Fabres cites 2 cases in which malignant diphtheria developed rapidly. The patients died on the third and fourth days, respectively, the first in spite of having been given from 500 to 1,000 units of serum per kilogram. He describes a foul

dark exudate extending to the mouth and nose, with hemorrhages and adenopathy, and also tachycardia, hypotension, marked pallor and tender, enlarged liver.

He claims that the low level of the cholesterol in the blood is due to an insufficiency of the adrenal cortex.

SCHLUTZ, Chicago.

MENINGOCOCCIC MENINGITIS. R. INFANTE and L. CID, Rev. chilena de pediat. **8**:659 (Nov.) 1937.

Infante and Cid present 2 cases of a condition diagnosed clinically and bacteriologically as meningococcic meningitis, one occurring in a premature infant and the other in a 2 year old child. The treatment consisted in intramuscular and intraspinal injections of serum, repeated lumbar punctures, hydrotherapy and administration of sedatives. Both patients recovered without complications or sequelae.

SCHLUTZ, Chicago.

PERTUSSIS VACCINE. STEEGER, Rev. chilena de pediat. **8**:663 (Nov.) 1937.

From observation of the effects of pertussis vaccine in 4,000 children Steeger believes that it is useful. In discussing its use he emphasizes phase I of the organism, large doses (from 8 to 10 cc.), dry sterilization of the needle and syringe, deep hypodermic injections and good refrigeration of the vaccine. The Sauer method is used.

Agglutination tests are not useful because of the autoagglutinative and nonspecific agglutinating properties of the organism.

SCHLUTZ, Chicago.

LYMPHADENITIS AND NEPHRITIS IN SCARLET FEVER. J. WOLFF, Monatschr. f. Kinderh. **71**:310 (Dec.) 1937.

Wolff has made the discovery that lymphadenitis and nephritis are complications of scarlet fever and develop from the tenth to the twenty-eighth day of the disease. The lymphadenitis is usually benign. When the nephritis progresses to uremia, he advises that the patient be given a carbohydrate diet and magnesium sulfate.

GERSTLEY, Chicago.

AN UNUSUAL FORM OF VASCULAR INJURY IN SCARLET FEVER. H. ZISCHINSKY, München. med. Wchnschr. **84**:1448 (Sept. 10) 1937.

Zischinsky previously reported 3 cases of nonnephritic edema complicating scarlet fever. In the third case cutaneous hemorrhages developed, from which the author concluded that the edema was due to vascular injury. Since then he has observed another similar case. Quincke described simple dropsy in scarlet fever in 1882 and in 1906 but made to mention of cutaneous hemorrhages. Zischinsky thinks that the condition is probably not uncommon but that it is incorrectly interpreted.

BRAHDY, Mount Vernon, N. Y.

RESULTS OBTAINED WITH PERTUSSIS VACCINE IN A HOME FOR INFANTS. O. SCHOTTDORF, München. med. Wchnschr. **84**:1868 (Nov. 9) 1937.

Schottdorf reports the results obtained with vaccine in 36 infants with whooping cough and 12 who were exposed to this disease. The vaccine contained the endotoxin, modified in such a way that it was not toxic though it retained its antigenic value. Several strains of pertussis bacilli were used in making the vaccine. There were from 4,000,000,000 to 8,000,000,000 organisms per cubic centimeter. The results depended on which stage of the disease was reached when treatment was started. The administration of three or four doses during the convulsive stage had little beneficial effect, but infants receiving injections during the catarrhal stage had a definitely lighter illness. When the injections were

given during the period of incubation, either very light pertussis developed or none at all. There were no local reactions, but some children showed a slight rise in temperature following the injection of the vaccine.

BRAHDY, Mount Vernon, N. Y.

CEREBELLAR ATAXIC FORM OF HEINE-MEDIN DISEASE. E. GLANZMANN, Schweiz. med. Wchnschr. **67**:972 (Oct. 9) 1937.

Glanzmann reviews the literature on the cerebellar ataxic form of poliomyelitis and describes 2 cases. The onset is generally slow, and the patients complain of fatigue usually in the legs and occasionally in the arms. The weakness in the legs becomes so severe that the child is either unable to walk or staggers when attempting to do so. The disorder may take its course without fever or with low fever. As the walk becomes more and more ataxic, a tendency develops to fall toward one or the other side. A tendency to fall backward is comparatively rare. Analysis of the ataxia in the author's cases revealed the absence of Romberg's swaying, but in a case reported by Wieland this symptom was present. The finger to nose experiment often fails; in the knee to heel test, the child finds the knee only after long searching, and in aiming movements past pointing with the hand and foot is observed. It is interesting that signs of meningeal irritation, which ordinarily are frequent in poliomyelitis, are absent in the cerebellar ataxic form. There is no rigidity of the neck or spinal sign, and even Amoss' sign may be lacking. Kernig's and Lasègue's signs are merely indicated. The four cardinal symptoms for the diagnosis of poliomyelitis fail completely in the cerebellar ataxic form. Of especial interest is the lack of localized paralysis of the extremities. The musculature of the back and of the extremities shows only surprising lack of tonus and more or less pronounced motor weakness. The cutaneous reflexes, particularly the abdominal and the cremasteric, are increased frequently and the plantar reflexes occasionally. This increase in the cutaneous reflexes seems to indicate irritation in the cerebral reflex arcs. The behavior of the tendon reflexes varies; they may be increased in both extremities or in only one and be reduced or abolished in the other. In the 2 cases reported the patellar and achilles tendon reflexes were abolished. Lumbar puncture reveals slight or no increase in pressure of the spinal fluid. The fluid is clear; the Pandy reaction is positive and the Nonne reaction usually negative. As regards the clinical course, the author says that complete cure is the usual outcome. That the cerebellar ataxic form is a type of poliomyelitis is proved by the fact that it occurs at the time of epidemics and that transitional forms exist. The author suspects that the process is localized in the brain stem and in the cerebellum.

EDITOR'S ABSTRACT. [ARCH. NEUROL. & PSYCHIAT.]

CULTIVATION OF SMALLPOX VIRUS ON THE CHORIOALLANTOIC MEMBRANE OF THE HEN'S EGG AND THE PREPARATION AND PRACTICAL USE OF SUCH CULTURES. I. PERAGALLO, Zentralbl. f. Bakt. (Abt. 1) **138**:310, 1937.

Peragallo cultivated the virus of vaccinia in tissue cultures, using both the method of Carrel and Rivers and that of Goodpasture and Woodruff. He found that the latter method was particularly useful and that the virus could be maintained serially with complete sterility. The virus seemed to be identical with that of cowpox in that Guarnieri bodies were demonstrable in the chorioallantoic membrane and in typical pustules formed in the skin of rabbits after injection of the culture virus. Culture virus conferred immunity to cowpox virus when injected into human beings, and the serums from these manifested neutralizing properties as long as two years after injection. Peragallo concludes that the cultivation of cowpox on the chorioallantoic membrane of the hen's egg is a practical method for the preparation of such material free from the dangers of bacterial infection and that the culture virus gives a solid immunity against cowpox in animals and in man.

CANNON, Chicago. [ARCH. PATH.]

EFFECT OF SCARLET FEVER SERUM ON THE COURSE OF FEVER AND COMPLICATIONS. E. G. JOFFE and K. M. HERMAN, J. Ukranian Sc. Inst. Maternal & Child Health, 1937, p. 28.

Scarlet fever antiserum affects only the patients whose condition is toxic and is without effect on those whose condition is septic. Serum should be injected as early as possible but may be helpful as late as the sixth day of the illness. It does not prevent complications. However, the complications in serum-treated patients were less severe than those in patients who did not receive treatment.

SEMENENKO-MCKHANN, Boston.

CEREBROSPINAL FLUID IN PERTUSSIS WITHOUT NEUROLOGIC COMPLICATIONS. J. H. MAGNUSSON, Acta pædiat. **20**:205, 1937.

The frequency of neurologic complications in cases of whooping cough is not yet ascertained. According to the statistics of several writers such complications occur with varying severity in between 6 and 14 per cent of cases of pertussis. Taken as a whole, neurologic complications lead to a high death rate: The outcome may be fatal in from 60 to 90 per cent of the cases. Divers classifications of these complications have been devised; these include convulsions, coma, central and peripheral paralysis, meningismus and psychic disturbances. Of these mishaps the commonest is convulsions. The genesis of pertussis eclampsia has not been clarified to general satisfaction. The best grounded explanations indicate one or more of the following elements: toxic encephalopathy, anoxemia and hemorrhage; also, activation of a predisposition to epilepsy or of latent tetany.

Some observers describe the occurrence of serous meningitis, with pathologic increase in the pressure, the cellular content and the protein of the cerebrospinal fluid. The evaluation of the significance of these findings in relation to convulsions requires that information be obtained concerning the state of the spinal fluid in cases of pertussis without neurologic complications. In this connection Levinson stated that the pressure of the cerebrospinal fluid is often increased in uncomplicated cases of whooping cough but that the increase is not accompanied by alteration of the protein concentration or of the cell count. Bayer's investigation of this point included 102 patients. He found an increase in the cells, with increase of pressure and of protein, with considerable frequency even though no neurologic disturbances could be demonstrated. However, Degkwitz, from whose clinic Bayer's paper appeared, criticized the latter's findings, stating that the selection of material had not been carried out properly. Other information relating to the matter has apparently not been published.

The author's investigations comprise 41 examinations of the spinal fluid in 33 patients aged 3 months to 7 years, who had pertussis in an active stage but exhibited no nervous manifestations; also, 16 examinations of the spinal fluid in 15 patients who showed some nonneurologic complication of the disease, e. g., otitis media or pneumonia. In no case were values for pressure, cell content, globulin or sugar encountered which definitely exceeded the physiologic range for healthy children.

MCCUNE, New York.

Acute Infectious Diseases

THE QUANTITATIVE NATURE OF IMMUNITY. P. S. RHOADS, Illinois M. J. **72**:503 (Dec.) 1937.

In this article Rhoads reviews various methods of immunization and cites his personal experiences and conclusions. In the giving of tetanus antitoxin, the time elapsed since the injury and the degree of contamination of the wound should be the determining factors in deciding on the dose. In the light of accumulating data, it seems likely that the present routine dose of 1,500 units for prophylaxis will give way to larger amounts. Very large doses of serum are advised for the active treatment of tetanus. It is too early to evaluate just how efficacious the

Ramon tetanus toxoid may prove to be. The Dick test is a reliable test for immunity to scarlet fever. The present method of the Dicks for active immunization against scarlet fever will immunize as large a proportion of persons whose reaction to the Dick test is positive as will an attack of the disease itself. In Rhoads' experience, no person immunized by this method to the point of giving a negative reaction has contracted scarlet fever. The majority of persons who received ricinoleated scarlet fever antigen or Veldee's toxoid did not become immune to scarlet fever. In the author's hands the prophylactic dose of scarlet fever antitoxin has been uniformly successful in passively preventing the disease. One therapeutic dose of the antitoxin is sufficient for treatment in the average case of scarlet fever. When the infection is severe, two therapeutic doses should be given. For persons highly sensitive to horse serum, human convalescent serum is the therapeutic agent of choice. Convalescent serum when used in large enough amounts is a useful prophylactic and therapeutic agent.

The Schick test is a reliable indicator of immunity to diphtheria if properly performed and properly interpreted. A control test with boiled Schick test material should always be made. Impotent Schick test material is a source of error. A more critical evaluation of the Schick test from the quantitative point of view is needed. As an immunizing agent diphtheria toxoid is superior to toxin-antitoxin. Rhoads believes that lasting immunity will be produced only if doses larger than those now in general use are given. The Schick test should be given every two years. Alum toxoid in the author's opinion has not been in general use long enough for an adequate evaluation of its effectiveness. In the active treatment of diphtheria the tendency is toward larger and larger doses of antitoxin.

BARBOUR, Peoria, Ill.

CONTROL OF RABIES. M. L. BLATT, Illinois M. J. **72**:520 (Dec.) 1937.

Blatt reports that 18,466 dog bites were reported in Illinois in 1936 and that 263 dog heads were examined during 1936 by the Illinois Department of Health, all of which were found positive for Negri bodies. A large number of the 18,466 persons bitten by dogs were treated with antirabic vaccine. Ten persons bitten by rabid dogs were unsuccessfully treated and died. Blatt considers such figures a challenge to the medical profession and public health agencies. A program by which rabies may be eradicated is cited.

BARBOUR, Peoria, Ill.

OCULAR MANIFESTATIONS OF BACILLARY DYSENTERY. TOULANT and SARROUY, Arch. d'opht. **53**:523 (July) 1936.

Bacteriologic uncertainty makes it difficult to individualize the ocular lesions accompanying the different varieties of dysentery. The authors consider the clinical aspect of the ocular lesions occurring in association with bacillary dysentery and their genesis. Scleroconjunctivitis is the most common lesion. This condition often appears with lesions of the joints and has its onset late, from ten to twenty days, and in cases of mild involvement even after the intestinal symptoms have cleared. It is self limited, treatment as a rule being unnecessary. Iritis and cyclitis are much more rare and occur later than conjunctivitis (from twenty to forty days). The authors report a case in detail. Other complications which have been reported include corneal ulcer, serpiginous ulcer, motor paralysis, choroidal hemorrhages and dacryoadenitis. Three hypotheses, i. e., the direct action of the dysentery bacillus, the effect of toxin and the effect of secondary infection, have been proposed to account for these complications.

MARLOW, [ARCH. OPHTH.]

PREVENTION OF INFECTIONS IN GROUPS OF INFANTS. P. LEREBOULLET, Rev. méd.-sociale de l'enf. **6**:2 (Jan.-Feb.) 1938.

The paper is introduced with a brief history of group care of infants in France and includes a delightful picture of nurses feeding infants asses' milk direct from

the source. To Victor Hutinel is given credit for first recognizing the special problems of infant care, and several of his aphorisms, which are just as true now as then, are quoted. The realization of the need for individual isolation of infants is credited to Hutinel. The article includes a discussion of some of the nurseries employing cubicle care, together with comment on the roles of the attendants and doctor.

DIETRICH, Beverly Hills, Calif.

MULTIPLE INFESTATIONS BY TAENIA SAGINATA. D. GREENWAY, An. Fac. de cien. méd. de La Plata **1**:23, 1937.

After reviewing numerous recorded cases of multiple infestation with Taenia saginata, in which from 2 to 27 tenias were noted in individual patients, Greenway gives an account of a subject who died of cancer of the adrenal and in whom 9 complete tenias were found massed in the small intestine. He comments on the colloquial reference to Taenia saginata as "solitaria" because of its occurrence as a solitary parasite in the immense majority of cases.

KALISKI, San Antonio, Texas.

SKIN MANIFESTATIONS IN RHEUMATIC FEVER. D. CORREA and O. MACCIO, Arch. de pediat. d. Uruguay **8**:752 (Dec.) 1937.

In 500 cases of rheumatic fever, Correa and Maccio five times observed the erythema of Besnier; in 4 of these cases the erythema coincided with cardiac involvement. One of the children died as a result of the rapid evolution of the erythema.

They also encountered 4 cases in which there were subcutaneous nodules, in 3 of which the nodules were associated with cardiac involvement. Nodular erythema was found in a single case.

SCHLUTZ, Chicago.

RHEUMATIC DISEASE IN CHILDREN IN URUGUAY. B. DELGADO CORREA, O. MACCIO and E. S. YANNUZZI, Bol. Inst. internac. am. de protec. a la infancia **12**:73 (July) 1938.

From a study of rheumatic disease in children it is obvious that not only is the percentage of children who have the disease increasing but the death rate also. There is an increased incidence of the forms which have a rapid evolution and are fatal.

Eighty per cent of the rheumatic children have not yet received suitable treatment.

The problem of rheumatism is equally pressing outside the hospital environment, as is demonstrated by the authors' researches among school children. In the school environment there is a relatively high percentage (28) of children showing rheumatic cardiopathy, although these children are considered healthy A strikingly high percentage (27) of the rheumatic children have rheumatic parents.

The struggle against rheumatism should engage both physicians and social workers.

EDITOR'S SUMMARY.

ACUTE RHEUMATIC INFECTION. E. KRAMAR, Rev. chilena de pediat. **8**:638 (Nov.) 1937.

Kramar notes an increase in the number of patients with acute rheumatic disease in his series, accompanied by a seeming change in the character of the disease. About 24 per cent of his patients are under 6 years of age. Cardiac involvement and usually polyarthritis occur early. Nodules and erythema annulare are seen frequently. He believes that the blood, heart and hemopoietic organs are affected simultaneously, since anemia of an aplastic form is marked. Simple hepatitis is frequent, a result probably of rheumatic rather than of intercurrent infection.

The treatment includes administration of large doses of aminopyrine, repeated small blood transfusions, hygienic care and injections of liver for anemia. Heavy metal preparations, sulfanilamide and streptococcus vaccines have produced poor results.

SCHLUTZ, Chicago.

TETANUS. A. JOHOW, Rev. chilena de pediat. **8**:654 (Nov.) 1937.

Johow reports 2 cases of tetanus: (1) that of a boy who had a puncture wound of the foot, in which an abscess developed, which was operated on, and (2) that of a girl who had had an operation to correct a weakness of the foot. Both patients had fever, trismus, risus sardonicus and abdominal cramps. The treatment consisted in intracarotid and intramuscular injections of antitetanus serum 10 cc. by the first route and 100 cc. by the second.

The author attributes the recovery of both children to the large doses of serum and to the intracarotid method used. No mention is made of the number of units used.

SCHLUTZ, Chicago.

USE OF AN ANTIVIRUS FOR GRIP IN YOUNG INFANTS. A. A. DORMIDONTOV and N. J. NELEPENKO, Pediatriya, 1937, p. 82.

The use of an antigrip virus prepared at the Metchnikov Institute as a prophylactic agent against grip gave only insignificant results in infants. The treatment of grip with the antivirus was completely unsuccessful.

SEMENENKO-MCKHANN, Boston.

EXPERIMENTS IN CONNECTION WITH SOME UNSOLVED QUESTIONS IN THE EPIDEMIOLOGY OF WEIL'S DISEASE. P. H. VAN THIEL, Nederl. tijdschr. v. geneesk. **81**:6106 (Dec. 25) 1937.

At the height of the swimming season Leptospira icterohaemorrhagiae can keep alive in free surface water for at least twenty-two days, with complete maintenance of virulence. In the vicinity of mud or in water heavily contaminated with urine the organisms can keep alive without loss of virulence for at least seven days; in mud they keep their virulence for at least five days. If a bathing establishment is screened by a wooden partition placed at the top levels with a view to prevent invasion by rats, this measure will not prevent the entrance of leptospiras excreted by rats outside the establishment. Strains of L. icterohaemorrhagiae which are practically avirulent are as able as virulent strains to infect guinea pigs. Likewise the saprophytic Leptospira pseudoicterogenes can invade the animal organism. Though epidemiologic data do not indicate that human infection with Leptospira canicola occurs during bathing, this may occur under special circumstances just as with L. icterohaemorrhagiae. In connection with experiments on guinea pigs it is supposed that a human infection with a small number of avirulent organisms of L. icterohaemorrhagiae will be protective against a minute infection with virulent leptospiras of the same species only if there is a response of the organism to this immunizing infection by detectable formation of agglutinin or of lysin in the serum.

VAN CREVELD, Amsterdam, Netherlands.

PNEUMOCOCCIC INFECTIONS IN CHILDREN. J. VAN LOOKEREN CAMPAGNE, Nederl. tijdschr. v. geneesk. **82**:2393 (May 14) 1938.

The provisional results of a study of pneumococci in 68 children in the hospital for children at Groningen, Netherlands, are given. The figures, though small, show agreement with those given in American statistics on the incidence of the various types of pneumococci in children. Only type XIV of Cooper, which is so important in America, was absent.

It was confirmed that in older children with lobar pneumonia type I is most frequent, especially if empyema complicates the condition, and that in pneumococcic

bronchopneumonia occurring in the first two years of life the types of Cooper are the cause. Quick diagnosis of the pneumococcus type as a preliminary to serum treatment of pneumonia in children is, in the author's opinion, important only if type I is found and bacteremia is present.

CREVELD, Amsterdam, Netherlands.

Chronic Infectious Diseases

OBSERVATIONS ON THE DEVELOPMENT OF INTRATHORACIC CALCIFICATION IN TUBERCULIN-POSITIVE INFANTS. M. BRAILEY, Bull. Johns Hopkins Hosp. **61**:258 (Oct.) 1937.

A series of 158 children, 65 of whom were white children and 93 Negroes, were found to be infected with tuberculosis before they had reached the age of 2 years. They have been kept under roentgen observation for periods ranging from a few months to more than five years. They afford material for a study of intrathoracic calcification.

It was found that calcification had appeared in the chest in about 17 per cent of children observed one year after the discovery of tuberculous infection. This proportion rose to 47 per cent by the end of two years, to 62 per cent by the end of three years and to 66 per cent by the end of four years.

The chests of white and Negro children became calcified at equal rates, but 55 per cent of the Negro children had unhealed lesions associated with the first calcification, as compared with 30 per cent of the white.

The proportion of children in whom calcification occurred varied with the extent of the lesion. Within a four year period, calcification was observed in 86 per cent of children who had shown a parenchymal lesion, in 67 per cent of those who had shown definite involvement of tracheobronchial nodes without a parenchymal lesion and in 36 per cent of those for whom no definite lesion had ever been recorded.

In 90 per cent of the patients calcification appeared first in the tracheobronchial lymph nodes. Calcifying pulmonary nodules were observed simultaneously in about a third of these children, and in another third pulmonary nodules appeared later.

About a fifth of the children in whom calcification developed had shown no definite lesion in earlier roentgenograms. In the remaining four fifths, calcification usually took place on the side of the thorax where the active lesion had been noted, but in 9 per cent it appeared only on the opposite side, where no lesion had been seen.

Serial roentgenograms demonstrate that a small deposit of calcium may become indistinguishable with time, owing to changes in the calcified mass or to its becoming hidden by mediastinal structures. An instance is cited of the absorption and disappearance of a calcified parenchymal nodule within four years after its first appearance.

Forty-six of the patients in this series, in whom calcification had been noted more than two years previously, were tested with old tuberculin. With the possible exception of a child who failed to react to 0.01 mg. and was not retested, none revealed loss of allergy. However, in a child not included in the present series allergy was shown to be greatly diminished as early as one year after intrathoracic calcification was first recorded.

FROM THE AUTHOR'S SUMMARY.

CONGENITAL SYPHILIS (A THREE YEAR SURVEY IN SYRACUSE). C. G. MURDOCK, New York State J. Med. **37**:1635 (Oct. 1) 1937.

There have not been enough surveys of congenital syphilis to give a true picture of its incidence. Routine performance of the Wassermann test on pregnant women should be required by law. The percentage of syphilitic pregnancies in Syracuse, N. Y., was found to be 3.8 in women observed in the clinics, 1.5 in

those seen in general practice and 0.5 in those under the care of the obstetrician. Of the 10 general practitioners doing the bulk of the obstetric work in Syracuse, 4 did not do the Wassermann test as a routine. AIKMAN, Rochester, N. Y.

A CASE OF CONGENITAL TUBERCULOSIS. D. PRICE, Brit. J. Tuberc. **31**:264 (Oct.) 1937.

Two routes have been described by which infection may reach the infant in cases of congenital tuberculosis: It may proceed from a tubercle in the placenta, via the umbilical vein to the liver, which becomes the seat of the primary focus in the fetus. Or it may enter in inhaled or ingested amniotic fluid, the bacilli finding primary lodgment in the lung or in the digestive tract. In the case described, that of an infant dying when 49 days old, the former route was taken by the infection, as evidenced by the following postmortem observations:

The hepatic gland was larger by far than all other caseous glands (especially the bifurcation gland), thus placing the site of primary implantation in the portion of the liver to which the maternal blood first gains access. Primary infection of the liver must take place in utero.

The bacilli causing lesions in the lungs were recognized as blood borne by (*a*) the transitional stages between miliary disseminations and the large foci and (*b*) the small size of the regional lymph gland.

In contrast to the case of congenital infection a case is reported of an infant with a typical primary complex in the lung, cavity formation in the primary complex and no other foci in the body who died at 8 weeks of age.

EUGENE H. SMITH, Ogden, Utah.

PATHOLOGIC CHANGES IN THE EAR IN LATE CONGENITAL SYPHILIS. O. MAYER and J. S. FRASER, J. Laryng. & Otol. **51**:755 (Dec.) 1936.

Mayer and Fraser show that the principal changes in the ear due to late congenital syphilis are osseous lesions, namely, osteomyelitis gummosa, periostitis gummosa and periostitis productiva. Other changes are usually caused by trouble in the bone which surrounds cavities and canals, invasion of which is easy. Thus the authors found serous labyrinthitis, either florid or cured, in the cochlea and vestibule in all patients examined. This was probably due to the setting up by miliary gummas in the labyrinthine endosteum of a serous exudation leading to slight proliferation of tissue in the scalae, ectasia of the ductus cochlearis and lastly, pronounced shrinking of the membranes, atrophy of the organ of Corti and degeneration of the maculas. In the semicircular canals the authors found chiefly productive inflammation developing in the periosteal layers. Constant endosteal proliferation of tissue and bone leads to concentric narrowing of the lumen. The endolymphatic space usually remains patent, and the endolymph flows freely. More rarely, a gummatous inflammation, consisting of miliary gummas or large ones which fill the entire canal, accompanies this periostitis productiva. This syphilitic tissue may erode the semicircular canal on the interior, thus causing eruptions into neighboring marrow spaces. Gummatous osteomyelitis leads to extensive changes of structure in the capsule of the labyrinth. The process attacks preferably the region of the semicircular canals at the margin of the periosteal capsule but invades the labyrinth. Deficient replacement of the resorbed bone may lead to osteoporosis of all the bones of the ear and of the petrous portion of the temporal bone. In the ossicle osteomyelitis generally causes ankylosis of the malleoincudal joint. In the oval window the authors found formation of osteophytes. There was no stapedial ankylosis, but specific infiltration of the annular ligament may have caused softening. In the os tympanicum there were gummas, necrosis of the bone and consequent cholesteatoma in the external meatus. The nervous system showed lesions due to miliary gummas in the ganglion spirale and to gummatous inflammation in Rosenthal's canal and the internal meatal fundus, particularly in the central and the superior fovea. The disorder is extremely insidious. In all cases observed the authors met fresh inflammatory processes, in

spite of the duration of the disease; particularly, subendosteal periostitis in the semicircular canals seems to flare up again and again. Fresh lesions are to be seen close to healed ones. Lesions may be caused anywhere while others nearby may subside. This explains the lack of uniformity of the clinical results, particularly in those revealed by functional examination of the labyrinth.

EDITOR'S ABSTRACT [ARCH. OTOLARYNG.]

SUN BATHING IN TUBERCULOSIS: ITS USE AND ABUSE. B. HUDSON, Tubercle **19**:72 (Nov.) 1937.

The value of sun bathing in the treatment of localized surgical tuberculosis is well established, but its indiscriminate use in the treatment of other forms of the disease may be correspondingly harmful. Patients with pulmonary tuberculosis should never be allowed to take a sun bath, since this is capable of lighting up unsuspected and latent foci. Proper sun treatment consists in gradual exposure of the body to the light, not the heat, of the sun, with proper circulation of free air. Most of the ill effects of improper sun bathing are due to the heat. As is true of other therapeutic measures, heliotherapy should always be supervised and controlled by a physician.

EUGENE H. SMITH, Ogden, Utah.

PALPEBRAL MANIFESTATIONS IN DELAYED HEREDITARY SYPHILIS. R. GOZBERK, Ann d'ocul. **174**:837 (Dec.) 1937.

Delayed hereditary syphilis often gives rise to such ocular lesions as keratitis, iritis iridochoroiditis and neuritis but localization of the lesion at the site of the lids is exceptional. Laurence reported a case in which signs of hereditary syphilis were present on the lids, lips and cheeks of a boy of 14 years. In 1888 Hutchinson described palpebral commissures, and von Michel in 1900 reported a gumma on the upper lid of a girl of 11 years. Other similar reports are recorded.

Delayed manifestations appear during childhood, adolescence and adult life. As a rule they develop spontaneously, but they sometimes appear during convalescence from infectious diseases or after trauma. Except in rare cases, these late appearances coexist with congenital dystrophies, which are of aid in making a diagnosis. Delayed hereditary syphilis may attack any part of the lid (skin, conjunctiva, subcutaneous tissue and tarsus). It appears in one of three forms: cutaneous gumma, subcutaneous gumma and gummatous infiltrations bordering on ulceration. The ulcerations may be so extensive as to bring about destruction of the lid.

Two cases are reported. The first was that of a boy of 11 years in whom a subcutaneous gumma developed in the parts surrounding the eye after an injury. In a few weeks an ulcerative process developed, causing irreparable mutilation of the lid. In the second case, that of a man of 30, syphilitic gummas appeared on the lid and on the face. In this patient, who was insufficiently treated, an injury revealed the latent syphilis. Two illustrations and a bibliography accompany the article.

MCKEE, Montreal, Canada. [ARCH. OPHTH.]

INFORMATION BASED ON THREE HUNDRED AND FORTY-NINE CASES OF HEREDOSYPHILITIC KERATITIS. D. LAZARESCU, Arch. d'opht. **53**:756 (Oct.) 1936.

This report is a statistical study of 349 cases of interstitial keratitis. According to the author this condition occurs in more than 4 per cent of patients with ocular disease. In 76.8 per cent of the cases of heredosyphilitic keratitis the patients were between 5 and 20 years of age. The condition was unilateral in 32.4 per cent. Four per cent of the patients had acquired syphilis. A history of abortion was given by 25.6 per cent of the mothers. Stigmas of inherited syphilis were present in 77 per cent of the entire group. The Wassermann test was positive in 83.3 per cent. At the time of the patient's admission to the hospital the disease was unilateral in 101 and bilateral in 248. In 57 cases the appearance of the second eye was not noted. In 80 cases both eyes were affected simul-

taneously. The average time between the attacks in the two eyes was one hundred and nine days. The conclusions drawn are as follows: 1. The most frequent signs of congenital syphilis are bone lesions (38 per cent) and Hutchinson's teeth (36 per cent). 2. Antisyphilitic treatment often prevents or delays involvement of the second eye (87 per cent). 3. Trauma is capable of causing an inflammation limited to one eye. Visual results were not determined in this series of cases.

S. MARLOW. [ARCH. OPHTH.]

ORGANIZATION AND FUNCTIONS OF PREVENTIVE MEASURES AGAINST TUBERCULOSIS IN CHILDHOOD. L. BETHOUX, Rev. de la tuberc. **3**:584 (May) 1937.

Preventive measures against tuberculosis in the child should begin with examination of the prospective mother. This prenatal prophylaxis, to be effective, requires that every pregnant woman be rigorously investigated for possible latent or active tuberculous disease and that suitable treatment be instituted if she is found infected. Postnatal prophylaxis obviously has to deal specifically with the infected mother and with the environment of the child during the first few years of life. Final success will depend on the promptness with which the child is removed from contact with infected persons. Separation of the infant from the infected mother is imperative. According to the author's plan, all infants of tuberculous mothers should first be placed in prophylactic or observation centers where, after careful examination and observation over suitable periods of time, they could be classified for further and more prolonged care and protection. Eventually they should be separated into the following groups: (1) those found nonallergic, roentgenologically normal and clinically healthy; (2) those found allergic but roentgenologically normal and clinically healthy; (3) those found allergic, roentgenologically suspect and clinically doubtful but with sputum and stomach contents negative for tubercle bacilli, and (4) those roentgenologically, clinically and bacteriologically tuberculous.

The children falling into the first two groups should be placed with rural families according to the Grancher plan. For those in group 3, preventorium care is necessary until it is determined whether the condition is to become stabilized or progressive. The fourth group should have sanatorium care, as well as those of group 3 whose process becomes progressive. Bethoux describes in some detail the ideal care of the children in these several categories, which in practice would indeed bring about not only a diminution of infantile morbidity and mortality but also a reduction in the incidence of pulmonary tuberculosis in adolescents and adults.

EUGENE H. SMITH, Ogden, Utah.

BACTERIOLOGIC DIAGNOSIS OF PULMONARY TUBERCULOSIS IN CHILDREN BY EXAMINATION OF THE GASTRIC CONTENTS: A STATISTICAL STUDY. P. F. ARMAND-DELILLE and KERAMBRUN, Rev. de la tuberc. **3**:626 (June) 1937.

Investigations of 1,298 children, covering a period of nine years, are summarized in this paper. Of this group, 712 presented definite evidence of tuberculous infection or signs arousing a suspicion of its presence. Tubercle bacilli were found in the gastric contents of 57 per cent of 594 children suffering from pulmonary tuberculosis of the primary or of the reinfection type, in 7 per cent of 38 who had infection of their bronchial glands, in 13.5 per cent of 36 with serofibrous pleurisy and in 4.1 per cent of children with bronchiectasis. Two patients with infected gastric contents were found among the remaining 582 children who showed no evidence of pulmonary tuberculosis. To clarify their findings further, the authors subdivided the group according to the particular type of infection found and describe in brief the clinical findings in the cases in which tubercle bacilli were found in the stomach contents.

On the technical side, the Löwenstein method of culture has proved of great value in the isolation of organisms from the homogenized stomach contents. By this means it is possible not only to increase the number of positive infections found but also to differentiate true tubercle bacilli from pseudoforms.

EUGENE H. SMITH, Ogden, Utah.

INADEQUATE PROPHYLAXIS AGAINST TUBERCULOSIS IN CHILDREN'S GROUPS. E. BERNARD and P. LAFOSSE, Rev. de la tuberc. **3**:812 (July) 1937.

Laxity in the medical examination of the personnel of schools and orphanages is decried by these authors. There have come under their observation a number of persons variously employed in such institutions, all of whom suffered from open tuberculous disease. Investigations carried out in institutions employing such persons showed an increased incidence of tuberculous infection in the children under their care. To remedy this situation it is urged that the personnel of all schools and child-caring institutions should be given each year a complete medical examination with roentgenologic control, and that all children in schools and other institutions where children are cared for should be given cutaneous tuberculin tests at frequent intervals.

EUGENE H. SMITH, Ogden, Utah.

TRANSMISSION OF CONGENITAL SYPHILIS TO A CHILD FROM A MOTHER INFECTED LATE IN PREGNANCY. P. BRUSA, Lattante **8**:463 (Aug.) 1937.

Brusa reports 4 cases. In the first the mother was probably infected about seventy days before parturition and showed signs of secondary syphilis and a positive Wassermann reaction six days after the child was born. The infant seemed healthy at the age of 6 days but at 2 months of age gave a positive Wassermann reaction and showed the following clinical signs of syphilis—anemia, snuffles, enlargement of the spleen and enlargement of the liver.

In the second case the infection occurred forty-six days, and in the third thirty days, before the child was born. In neither did the child show clinical or serologic signs of congenital syphilis.

In the fourth case the infection took place twenty-three days before the birth of the child. The child showed no signs of syphilis at 9 days of age but at 4 months of age showed the characteristic anemia, coryza and enlargement of the liver and spleen; the Wassermann reaction was positive. The theory is presented that infection of this child took place in utero by contact with the infected sperm of the father.

HIGGINS, Boston.

THE FAMILY HISTORY OF SYPHILITIC INFANTS. P. BUXÓ IZAGUIRRE, An. de pediat. **2**:158 (March) 1935.

In the past five years clinical manifestations of syphilis have not been seen in infants as before, owing to the intensive treatment given to mothers even though they presented no symptoms except a positive Wassermann reaction. Infants of treated syphilitic mothers often appear healthy, and only several years later do specific lesions develop. Also, frequently children of syphilitic mothers who have had intensive antepartum treatment are born completely healthy. The authors have studied the histories of 100 children of syphilitic parents, including data on the parents and siblings, and compared these infants with a similar control group of 100 children of nonsyphilitic parents. Of each infant there is noted briefly the family history, the type of labor, the weight at the first visit, the progress and the Wassermann reaction. A summary of the analysis follows:

	Syphilitic Group	Normal Group
Premature infants	25	1
Dead and macerated fetuses delivered from fifth to ninth month	55	1
Fetuses aborted under 5 months	55	32
Infants showing illness in first month of life	21	17
Siblings who died	104	47

It is noteworthy that while in the syphilitic group there were 5 with specific cutaneous lesions, 1 with congenital malformation and 4 with other lesions apparently specific, the normal group showed no suspicious lesions of the skin.

Emphasis is placed on the importance of diagnosis. It is often difficult to diagnose syphilis in infants with no clinical signs and no specific serum reactions in the first month and in infants of mothers who had intensive antepartum treatment. A family history of a macerated dead sibling is almost absolute proof of syphilis in the parents.

GIFFEN, Toledo, Ohio.

TUBERCULOSIS OF THE NURSLING. H. MAGLIANO and F. J. ROCA, An. Soc. de peuricultura de Buenos Aires **3**:33 (Jan.-March) 1937.

The authors present 3 cases of tuberculosis in young infants and stress the need for cooperation between the various organizations in order to eradicate tuberculosis.

HERRON, Monroe, La.

TRAUMATIC PARENCHYMATOUS KERATITIS IN CONGENITAL SYPHILIS. G. VON GROLMAN, Arch. de oftal. de Buenos Aires **12**:449 (July) 1937.

A case of severe parenchymatous keratitis developing after a contusion is reported. After several weeks the cornea began to clear and finally cleared entirely. Shortly afterward, the other eye became affected with typical parenchymatous keratitis, which ran the usual course. There was a 4 plus Wassermann reaction.

Von Grolman discusses at considerable length the different opinions as to the relation of trauma to syphilitic lesions in general and to those of the eye in particular. He also discusses the theory that parenchymatous keratitis is not an essentially syphilitic lesion, the syphilis being a predisposing cause (Kümmel). The author is inclined to accept this view.

FINLAY, Havana, Cuba. [ARCH. OPHTH.]

POTT'S DISEASE WITH AN UNUSUAL COURSE. R. G. MENDOZA and A. NAVARRETE, Bol. Soc. cubana de pediat. **9**:473 (Nov.) 1937.

The authors report a case of Pott's disease of the cervicodorsal type in a 3 year old boy. The lesion caused total destruction of the seventh cervical and first dorsal vertebrae and partial destruction of the second and third dorsal vertebrae, with formation of an abscess. The physical deformities and functional symptoms were not marked. The roentgenogram was atypical. The abscess invaded the meninges, pleura and lungs and became infected secondarily as a result of communication with the exterior through the bronchi, with the result that a pyopneumothorax developed.

There was a total absence of nervous symptoms in spite of the invasion and destruction of the meninges.

SCHLUTZ, Chicago.

TUBERCULOUS AND ORDINARY PNEUMONIA. C. H. MIYARES, Bol. Soc. cubana de pediat. **9**:521 (Dec.) 1937.

Miyares presents a case of pneumonia which he studied clinically and by means of roentgenograms. The Mantoux test, smears of the gastric fluid and animal inoculations repeatedly gave negative results. A diagnosis of nontuberculous pneumonia was made. Miyares states that clinical, roentgen and blood examinations may not differentiate the two types. Repeated tuberculin tests at long intervals if persistently negative rule out tuberculosis. Bacteriologic studies of the gastric juice, with animal inoculations and cultures, are important.

SCHLUTZ, Chicago.

TUBERCULOUS OTITIS MEDIA IN AN INFANT. G. CARDELLE and F. BORGES, Bol. Soc. cubana de pediat. **9**:533 (Dec.) 1937.

Cardelle and Borges present a case of tuberculous otitis media in a 5 month old infant who had had colds and fever for three months, anorexia, loss of weight,

diarrhea and vomiting. Otitis media developed, with palsy of the left side of the face. The aural discharge and gastric contents were positive for Koch's bacillus. Autopsy revealed miliary tuberculosis.

Tuberculous otitis media is frequent in children but often is not diagnosed, as it may have an acute beginning and be marked by secondary invaders. The authors suggest a careful study for tuberculosis in otitis media of long standing. Facial palsy is an important symptom.

SCHLUTZ, Chicago.

CONGENITAL SYPHILIS IN INFANCY. P. ARAYA, Rev. chilena de pediat. **8**:625 (Nov.) 1937.

Araya describes a type of congenital syphilis in which hemorrhages of the skin and of the umbilicus occur. He attributes these to severe capillary disturbances, such as stagnation due to cirrhosis or to infection. He believes that fetal syphilis is a visceral form and that it is serious since it affects almost all organs.

He describes the various visceral lesions. Hepatomegaly occurred in 20 per cent of his series, while splenomegaly was more constant. Syphilis should be suspected in unexplained splenomegaly.

He describes Parrot's pseudoparalysis, which must be differentiated from osteomyelitis and from arthritis.

SCHLUTZ, Chicago.

PRIMARY TUBERCULOSIS WITH SPONTANEOUS PNEUMOTHORAX AND SUBCUTANEOUS EMPHYSEMA. F. ROSSELLO and A. R. DUTRUEL, Rev. Soc. de pediat. de Rosario **2**:205 (Oct.) 1937.

Spontaneous pneumothorax and subcutaneous edema developed in a 15 month old child after an infection of forty days' duration. An excellent roentgenogram is shown.

SANFORD, Chicago.

MILIARY TUBERCULOSIS IN AN INFANT WITH RECOVERY. E. STRANSKY, Rev. Soc. de pediat. de Rosario **2**:248 (Oct.) 1937.

The child had miliary tuberculosis, as shown by roentgenograms. Cutaneous tuberculids developed, and the child recovered. In view of this favorable outcome the author believes that the cutaneous infection exerted a favorable action on the general condition.

SANFORD, Chicago.

HOW INFECTIOUS IS CHILDHOOD TUBERCULOSIS FOR CHILDREN? RIETSCHEL, München. med. Wchnschr. **84**:1862 (Nov. 19) 1937.

The course of tuberculosis in children depends on (1) the number of bacilli with which the child is infected, (2) the frequency of exposure to infection and (3) the constitution of the child. The initial infection is usually subpleural and benign. However, massive infection, although it is infrequent, is dangerous. Repeated infections before sufficient immune response has developed in the body are also dangerous. Concerning the varying virulence of tubercle bacilli, nothing is known.

The infection in infants is usually pulmonary. The lesion is exudative and caseates rapidly. In this stage the patient spreads tubercle bacilli and is dangerous as a companion to other children. In older children the infectiousness depends on the stage of the disease. The primary development is short and usually runs its course before a diagnosis is made. In the second stage of Ranke the infection becomes more generalized. At this time, especially during the second and third years of life, the patient disseminates tubercle bacilli, and every effort should be made to isolate him. Children of school age without clinical symptoms are less likely to spread the disease. The third stage of Ranke is rarely seen in children under 10 years of age. Pulmonary phthisis usually occurs at puberty and requires immediate isolation.

The problem of prophylaxis is not to prevent every one from being exposed to tuberculosis but rather to expose the individual child at the proper time (not in the early years of life) to a minimal infection, which he can overcome and which leads to good immunity.

BRAHDY, Mount Vernon, N. Y.

USEFULNESS OF SEROLOGIC DIAGNOSIS IN TUBERCULOSIS. P. WEILAND, München. med. Wchnschr. **84**:1863 (Nov. 19) 1937.

Weiland has found the complement fixation and precipitin reactions helpful in the diagnosis of tuberculosis. He advises using them in differential diagnosis, in the examination of apparently healthy persons and in research work. After the clinical diagnosis has been established, the serologic tests are of little significance.

BRAHDY, Mount Vernon, N. Y.

SEDIMENTATION RATE IN CHILDHOOD ABDOMINAL TUBERCULOSIS. E. SOMMERFELD, Ztschr. f. Kinderh. **59**:303 (Dec. 24) 1937.

Characteristically, the sedimentation rate is normal or low in children with abdominal tuberculosis. Acceleration may occur if this condition is complicated with serous pleuritis, ileus, purulent *Durchwanderungsperitonitis* or hematogenous infection of extraperitoneal lymph nodes. Nine cases are reported in detail.

SIEMSEN, Chicago.

TUBERCULOUS PACHYMENINGITIS. O. KOCH, Ztschr. f. Tuberk. **78**:318 (Sept.) 1937.

Koch cites reports from the literature which indicate that tuberculous pachymeningitis is a process accompanying tuberculosis of adjoining organs and that it develops by contact. However, he observed still other forms of pachymeningitis. In this paper he gives attention chiefly to the relations between tuberculous leptomeningitis and tuberculosis of the brain, on the one hand, and tuberculous inflammation of the dura, on the other. There is reason to assume that tuberculosis of the pachymeninx may develop after that of the leptomeninges, simultaneously with it or even before. There is, in other words, an independent, hematogenically metastasizing tuberculous process of the dura mater. The author differentiates three types: 1. Internal tuberculous pachymeningitis, which develops by contact infection. The most frequent form of this type, the fine nodules that accompany tuberculous leptomeningitis, has been described before, particularly by Huebschmann, who emphasized that this form of nodular tuberculosis of the dura is not seen in all cases of tuberculous leptomeningitis. It is often absent in cases of recent tuberculous basal meningitis. It is difficult to say in what stage of development the leptomeningitis must be in order to produce infection of the dura. 2. Tuberculous pachymeningitis in which the dependence on tuberculous processes in the leptomeninges is possible but not proved. Koch reports 3 cases. In 2 there existed, in addition to the changes in the dura, numerous solitary tubercles of the brain, in the third case they were absent. 3. Independent hematogenic metastasis. In one case the brain could be lifted from the two large tubercles of the dura without loss of substance. The corresponding portions of the brain showed depressions that were entirely smooth and were still covered with pia mater. Thus, it cannot be said that the tuberculomas had been torn from the brain and adhered only to the dura. There also existed a tubercle in the substance of the brain, but this was nowhere in contact with the surface, so that it could not give rise to an infection of the dura and the leptomeninges. Koch regards tuberculomas of the dura as independent hematogenic metastases caused by the same dissemination as the tubercle in the brain itself. He cites a case in which there existed a tubercle only of the dura, all other parts of the brain being free from tuberculosis. Finally, he describes a form of tuberculosis of the meninges that developed in the course of primary tuberculosis in a child. In this case microscopic examination disclosed extensive changes in all layers of the dura and also in the leptomeninges.

EDITOR'S ABSTRACT. [ARCH. NEUROL. & PSYCHIAT.]

Diseases of Blood, Heart and Blood Vessels and Spleen

CONGENITAL CARDIAC MALFORMATION PRESENTING COMPLETE INTERRUPTION OF THE ISTHMUS AORTAE WITH TRANSPOSITION OF THE GREAT ARTERIES. L. P. HAMBURGER JR., Bull. Johns Hopkins Hosp. **61**:421 (Dec.) 1937.

An unusual congenital cardiac malformation is presented, in which complete interruption of the aortic arch is associated with transposition of the great arteries. A review of the literature discloses 13 cases of complete atresia of the isthmus aortae. In only a single instance was there also transposition, and this one was complicated by a large defect of the interventricular septum and persistence of the ostium primum.

FROM THE AUTHOR'S SUMMARY.

DOES LIVER SUPPLY FACTORS IN ADDITION TO IRON AND COPPER FOR REGENERATION OF HEMOGLOBIN IN NUTRITIONAL ANEMIA? E. B. HART, C. A. ELVEHJEM and G. O. HOHLER, J. Exper. Med. **66**:145 (Aug.) 1937.

The authors reiterate that according to present knowledge the nutrients needed for maximal regeneration of hemoglobin in uncomplicated secondary anemia are iron, copper and amino acids for the construction of the protein part of the hemoglobin molecule.

In spite of these facts, and probably because liver is such a valuable material for the treatment of pernicious anemia, great emphasis has been placed on the use of liver and liver products in the treatment of secondary anemia.

The authors experimented with rats and came to the conclusion that the effectiveness of whole liver in the treatment of nutritional anemia is directly proportional to its available iron and copper content. The other constituents in liver are not needed for maximal regeneration of hemoglobin on a diet of milk, iron, copper and manganese.

Commercial preparations of liver with iron or iron and copper varied greatly in their hemoglobin-regenerating efficiency in rats with nutritional anemia. The variation was correlated directly with the iron and copper content of the preparation. When the copper-iron ratio was too wide the regeneration of hemoglobin was checked, although the iron supply was sufficient for optimal regeneration.

The authors point out that these facts do not detract from the nutritional value of liver extract, for there is ample evidence in the literature that this product is a most excellent source of most of the factors in the vitamin B complex. The facts do emphasize, however, the importance of recognizing the value and limitations of each ingredient in such mixtures. In the case of anemia due to a simple deficiency of iron and copper, which is the case in many children, small doses of iron and copper work efficiently without other additions.

KNICKERBOCKER, Dallas, Texas.

COOLEY'S ANEMIA. C. GABRIELE, Lattante **8**:595 (Nov.) 1937.

The report concerns a baby boy, one of twins, born of the mother's third pregnancy. Seven years previously the mother had malaria, from which she recovered in about two months; during the seventh month of the pregnancy in question she began to show progressive weakness and anemia, which became more marked as pregnancy progressed; she was given transfusions of blood and treatment with liver, iron, arsenic and quinine. The father and three other children, including the other twin, were perfectly well.

The child was fed by a wetnurse from birth. On the eighth day after birth jaundice was noticed, which was followed by pallor, anorexia and weakness. The child was brought to the clinic in Naples, Italy, at 1 month of age; the complaints were jaundice, anorexia, anemia and increase in the size of the abdomen. The child showed poor nutrition, marked pallor and slight icterus. There was no edema. On physical examination a very large spleen was detected, occupying almost all of the left side of the abdomen. The liver was slightly enlarged. The

red blood count was 960,000; the hemoglobin content was 22 per cent; the nucleated cells numbered 15,800, of which 8,960 were white cells and 6,840 were nucleated red cells; the leukocyte count included 23 per cent polymorphonuclear neutrophils, 2 per cent eosinophils, 1 per cent basophils, 68 per cent lymphocytes, 3 per cent monocytes and 3 per cent myelocytes. Biopsy on marrow of the tibia showed a more notable increase of the immature forms of the red cell series than of those of the white. Roentgen studies showed no osteoporosis. The van den Bergh test was positive (indirect); the cholesterol content of the blood was 90 mg. per hundred cubic centimeters; the Wassermann reaction was negative; the reaction to tuberculin was negative. On alternate days the child was given injections of a liver extract, each dose being equivalent to 250 Gm. of fresh liver. The child's condition is outlined in monthly reports. At the age of 5 months he was notably improved. The spleen was relatively much smaller, reaching only 2 finger-breadths below the costal margin. There had been a steady gain in weight, and the red cell count was 3,840,000, the hemoglobin content 74 per cent, the nucleated cells 8,380, of which 8,055 were white cells and 325 red cells. There were 28 per cent polymorphonuclear neutrophils, 2 per cent eosinophils, 1 per cent basophils, 60 per cent lymphocytes, 70 per cent monocytes and 2 per cent metamyelocytes. The child's general appearance, nutrition and blood indicated a clinical cure.

The author's diagnosis was Cooley's anemia, with an absence of osteoporosis and a clinical and hematic cure under liver therapy. HIGGINS, Boston.

ANATOMOPATHOLOGIC CHANGES OF THE SPLEEN IN ANEMIA. P. DE ELIZALDE, Arch. argent. de pediat. **8**:1093 (Nov.) 1937.

Elizalde describes erythroblastic anemia with an insidious course in a patient who was alive at the time of his report. A splenectomy was done, and comparisons were made with spleens removed at earlier ages, permitting a study of changes in the course of the disease. SCHLUTZ, Chicago.

SUBACUTE MYELOID LEUKEMIA IN AN INFANT. A. C. GAMBIRASSI and M. E. VARELA, Arch. argent. de pediat. **8**:1139 (Nov.) 1937.

Gambirassi and Varela present a case of subacute myeloid leukemia in an 18 month old boy who clinically showed the picture of lymphatic leukemia. The differentiation was made by hematologic studies and confirmed by biopsy and autopsy. SCHLUTZ, Chicago.

STUDIES ON SEDIMENTATION RATES WITH THE MICROMETHOD. A. CHATTAS, Arch. argent. de pediat. **8**:1256 (Dec.) 1937.

Chattas has studied 3,000 sedimentation rates by the micromethod since 1931 and says the usefulness of determining the sedimentation rate is equal to that of obtaining the temperature or the hematologic curve. He gives the advantages of the micromethod as well as the value of its use in various conditions and claims that it should be given the same value as any other diagnostic aid. The clinical observations are still the more important. SCHLUTZ, Chicago.

MALIGNANT ENDOCARDITIS AND PULMONARY STENOSIS. J. C. C. CALDERIN and J. M. LABOURDETTE SCULL, Bol. Soc. cubana de pediat. **9**:457 (Nov.) 1937.

A child had had a pulmonary stenotic lesion from early infancy and at the age of 11 years presented what seemed to be subacute malignant endocarditis. He died twenty-four days after the beginning of his last illness. The authors regarded the condition as congenital cardiopathy. The postmortem diagnosis was pulmonary stenosis, plastic valvuloparietal endocarditis and chronic pulmonary endarteritis, without malignant changes. SCHLUTZ, Chicago.

ERYTHROTRANSFUSIONS. E. G. CONESA and R. MONTERO, Bol. Soc. cubana de pediat. **9**:547 (Dec.) 1937.

The authors present a case of lymphoid leukemia in a 2 year old child. He was made temporarily polycythemic by transfusion of from 150 to 250 cc. of red blood cells every two days. No changes occurred in the leukemic picture. The patient was much improved when discharged.

The authors conclude from this study that transfusion of erythrocytes is valuable as symptomatic treatment in secondary anemia and has advantages over that of whole blood. With care, the transfusion does not cause vomiting, diarrhea or other reactions.

SCHLUTZ, Chicago.

A CASE OF WERLHOF'S PURPURA HAEMORRHAGICA. R. BERGALLO ANDRADE, Rev. Soc. de pediat. de Rosario **2**:208 (Oct.) 1937.

The condition was present in a 4 year old child. The blood platelets were reduced in number, and the bleeding time was prolonged, with no change in the coagulation time.

SANFORD, Chicago.

ERYTHROBLASTIC ANEMIA OF COOLEY. J. C. SANTA MARIA, J. P. PICENA and F. C. MILIA, Rev. Soc. de pediat. de Rosario **2**:231 (Oct.) 1937.

The red cell count was 1,230,000 and the hemoglobin content 20 per cent. Roentgenograms showed the typical cranial spindling.

SANFORD, Chicago.

INVESTIGATION OF BONE MARROW IN NURSLINGS. G. JOPPICH and P. LIESSENS, Monatschr. f. Kinderh. **71**:382 (Dec.) 1937.

Joppich and Liessens studied the bone marrow of normal nurslings. Specimens were obtained by 23 tibial punctures. They submit photographs. There is no great difference from the observations in the bone marrow of adults except for an increase in lymphocytic cells up to 57 per cent. These cells are probably mostly true lymphocytes, although a few may be monocytes or micromyeloblasts.

GERSTLEY, Chicago.

BLOOD TRANSFUSION IN INFANCY. J. SVEJCAR and E. POLAK, Časop. lék. čsk. **75**:373-377 (March 27); 414 (April 3); 447 (April 10) 1936.

The authors review 219 cases in which they used the intramuscular, intraperitoneal, intrasinous and intravenous methods. Their preference is for the last. The citrate method is preferred because of its contribution to ease of operation. Various formulas for estimating the amounts of blood to be used are discussed. About 20 to 25 cc. per kilogram of body weight has been used with no evidence of plethora. The reactions discussed are hemolysis, icterus, respiratory shock and urticaria. These were more prevalent in patients with sepsis and bronchopneumonia. No incompatibility was noted, but a premature infant with bronchopneumonia died of plethora and 2 patients with bronchopneumonia and sepsis with erysipelas, respectively, died of collapse. Ten per cent had elevation of temperature, 50 per cent of whom were suffering from sepsis, and a few had a morbilliform rash shortly after transfusion. The results are summarized as follows: Immediate improvement occurred in patients with haemophilia neonatorum (melena); in patients with milder hemorrhage, including intracranial hemorrhage, the intramuscular injections were used; in patients with alimentary and infectious anemias convalescence was markedly shortened; preoperative transfusion practically eliminated postoperative shock; in cases of nutritional dystrophy the death rate was reduced to 11 per cent; in cases of alimentary intoxication the death rate was lowered to 29 per cent, but in those cases in which this condition was complicated by infection the result was negligible; in cases of true sepsis transfusion may be

contraindicated and then fractional intramuscular injections are recommended; in the presence of bronchopneumonia which is not localized or in the presence of circulatory disturbance transfusion must be done cautiously because of possible plethora.

STULIK, Chicago.

STUDIES OF THE RESISTANCE OF THE CUTANEOUS CAPILLARIES IN CHILDREN. N. LINDQUIST, Acta pædiat. (supp. 2) **20**:1, 1937.

This 167 page monograph is based on a large amount of careful work carried out by the author in the University Children's Clinic, Lund, Sweden. Forty pages are devoted to a critical review of previous work in this field and 108 pages to a description of the author's investigations. Approximately 150 titles are listed in the bibliography.

Capillary resistance was examined by means of Hecht's cupping technic; tests were performed on 10 infants during each of the first twelve months of life and on an equal number of children during each of the first twelve years. Separate tests were made on each of several regions of the body. Resistance was found to vary with the age of the child, being highest during the first month of life and then declining until the end of the second year, when values were reached which persisted throughout the remainder of childhood. The resistance of the vessels in the various areas tested was fairly uniform in young infants; local variation became more obvious with advancing age. Hence, it was possible to predict from the values obtained in one region the values which would be found in other regions. Large individual variations were encountered among different subjects. The two sides of the body were demonstrated to be entirely symmetric.

Supplementary measurements were made on 108 newly born full term infants and on 22 prematurely born infants. Among other observations, the resistance was found to be distinctly lower in the premature than in the full term subjects.

The detailed presentation of the studies and the comment on the significance of the results do not lend themselves well to abstracting.

McCUNE, New York.

CONGENITAL HEART BLOCK. A. WALLGREN and S. WINBLAD, Acta pædiat. **20**: 175, 1937.

The first authentic case of congenital heart block was reported by van der Heuvel in 1908. The most informative reviews of the growing literature relating to this matter are those of Yater and his collaborators in the United States and of Nielsen in Scandinavia. Yater insists that an unequivocal diagnosis must fulfil the following postulates: 1. The heart block shall be established by graphic records to have occurred in a relatively young person. 2. Bradycardia must have been demonstrated at an early age. 3. There must be no history of an infection that might have been responsible for the heart block. Campbell and Suzman recognized the fact that in young children the combination of congenital malformation of the heart with attacks of syncope provides strong support for the assumption that there is congenital heart block; conspicuous bradycardia in a young subject is also highly suggestive.

The most recent tabulation of the reported cases was published by Nielsen in 1935; this lists 66 authentic cases. The present publication amplifies this number to 77 and includes reports of 2 cases observed by the authors. Reasons are given to support the surmise that the phenomenon is considerably more common than the number of published cases would indicate.

Both of the authors' patients were infants. In the first the congenital cardiac lesion was an expression of a familial abnormality: Five members of the family and near relations of the father had been shown to have organic heart disease; in 3 instances block was present. In the authors' 2 cases fetal bradycardia was observed before delivery. In the first case the dissociation between the auricle

and the ventricle was confirmed by fluoroscopic examination; in the second, by electrocardiogram. The first patient exhibited no clinical evidence of gross malformation of the heart; the infant died at the age of 10 months of an intercurrent infection. The second infant manifested cyanosis on exertion and had attacks of syncope; death occurred at the age of 3 months. In the first case autopsy showed the heart to be grossly normal; the bundle of His was interrupted for a short distance from the atrioventricular node by the fibrous tissue of the annulus fibrosus. In the second case the ventricular septum was patent, and the bundle of His was found only as a degenerated remnant, which lay in a strand of fibrous tissue and was separated both from the auricular muscle and from the normally developed portions of the ventricular conduction system. In the first patient the anomaly was regarded as of independent origin; in the second it was evidently correlated with failure of formation of the interventricular septum. The embryologic comment is informative and the bibliography serviceable.

McCune, New York.

Diseases of Nose, Throat and Ear

Differential Diagnosis Between Thrombosis of the Lateral Sinus and Acute Bacterial Endocarditis. H. Rosenwasser, Arch. Otolaryng. **26:** 668 (Dec.) 1937.

The author reports 5 cases in which a differential diagnosis had to be made between thrombosis of a lateral sinus and acute bacterial endocarditis. When the Ottenberg differential blood culture method shows a large number of colonies in cultures of blood from a jugular vein and from a peripheral vein in the arm, it points to endocarditis as the cause, whereas when a large number of colonies appear in cultures of blood from one or both jugular veins and many but considerably fewer colonies appear in cultures of blood from the arm it points to thrombosis of the lateral sinus. Sinus thrombosis is caused by none of the pneumococci except type III. Cutaneous embolic lesions occur almost exclusively in cases of endocarditis. Blurring of the margins of the disks, papilledema and other such changes in the fundus occur in 16 per cent of cases of sinus thrombosis. The importance of close cooperation of otologist, internist and bacteriologist in borderline cases is particularly stressed.

Greenwood, Chicago.

Clinical Observations on Tonsillectomized Cases. A. A. Cinelli, New York State J. Med. **37:**2079 (Dec. 15) 1937.

Cinelli gives the indications for tonsillectomy. Aikman, Rochester, N. Y.

Discussion on Otitis Media in Early Childhood (Under Five Years). J. Le Mée and others, Proc. Roy. Soc. Med. **30:**1293 (Aug.) 1937.

Otitis media in early childhood is discussed in detail by the following men: Dr. J. M. Le Mée, Mr. T. Ritchie Rodger, Dr. J. H. Ebbs, Mr. Stirk Adams, Dr. C. E. Scott, Dr. R. B. Lumsden, Dr. Douglas Guthrie, Mr. E. Watson-Williams and Dr. McNair Scott. Anatomic points in the production of otic infection, various types of involvement of the ear and of the mastoid, analyses of cases, statistical reports on the incidence of otitis media and sinusitis, the bacteriologic picture, the association of the disease with gastrointestinal disturbances and with pneumonia, its complications, prophylaxis, detailed reports of cases and the operative indications and technic are taken up. Personal views on many of these matters are expressed by the discussers, and some differences of opinion are noted. The subject is reviewed in an interesting and instructive manner.

Campbell, Philadelphia. [Arch. Otolaryng.]

CONGENITAL MALFORMATIONS OF THE EXTERNAL EAR. F. MARTILLOTI, Pediatria **45**:337 (April) 1937.

Martilloti describes 2 cases of congenital malformation observed in his clinic. After having reviewed the various embryogenic factors, he illustrates the necessity of utilizing roentgenograms in the study of such malformations inasmuch as they show in children indications of operability or of the functional capacity of the ear.

PALMIERI, Brooklyn.

INDICATIONS FOR AND RESULTS OF TONSILLECTOMY IN CHILDREN. C. P. MERCANDINO, F. OSCAMOU Y J. C., An. agrupacion med. del patronato de la infancia **1**:27, 1937.

This report is based on ten years' observation of 12,000 tonsillectomized children and a similar control group. The indications for the removal of tonsils were: mechanical obstruction in 14 per cent, frequent tonsillitis in 13 per cent, continuous colds with nasal discharge in 23 per cent, repeated otitis media in 9 per cent, cervical adenitis in 11 per cent, unexplained low fever in 2 per cent, frequent acute laryngitis in 3 per cent, persistent and repeated cough in 0.2 per cent, bronchitis in 8 per cent, dental caries with hypertrophy of the tonsils in 7 per cent, need for prophylaxis against asthma in 0.3 per cent, acute polyarticular rheumatism in 0.3 per cent, rheumatic endocarditis in 0.7 per cent, nephritis in 0.2 per cent, malnutrition associated with infections in 0.2 per cent and postinfectious diseases in 5 per cent.

To arrive at a conclusion as to the results of these operations the authors noted all the infectious diseases (e. g., tonsillitis, otitis media, adenitis, pneumonia, rheumatism, diphtheria, scarlet fever and tuberculosis) in the children operated on and in the children not operated on.

	Percental Incidence of Given Condition	
	Group Operated On	Group Not Operated On
Head colds	18.0	33.0
Pain in throat and tonsillitis	8.0	40.0
Cervical adenitis	6.0	14.0
Otitis media	14.0	38.0
Diphtheria	1.3	3.9
Scarlet fever	3.3	4.6
Rheumatism	5.0	33.0

The tabulation shows the favorable results of tonsillectomy. The unfavorable results were that chorea occurred more frequently in the group operated on and that the incidence of measles, laryngitis, malnutrition, bronchitis and pneumonia was not modified by tonsillectomy.

GIFFEN, Toledo, Ohio.

VESTIBULAR DISORDERS IN HEREDITARY DEAFNESS. E. MÜLLER, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **142**:156, 1936.

Müller points out that studies of other investigators have revealed that vestibular disturbances are more frequent in acquired than in congenital deafness. His own investigations, however, have revealed that concurrence of hereditary deafness and disturbances in the apparatus of equilibrium is not at all rare. He describes two unusual types of hereditary vestibular lesion, one of which he observed in a family with hereditary degenerative deafness and the other in a family with sporadic deafness. In the first family he observed in 4 deaf members of one generation a vertical nystagmus that was dependent on the position of the body. The children of both families showed considerable improvement of the hearing capacity. However, the functional impairments of the vestibular apparatus recurred in slightly changed form in the descendants.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

DIAGNOSIS AND THERAPY OF SECRETORY CATARRH OF THE MIDDLE EAR, WITH ESPECIAL CONSIDERATION OF PUNCTURE OF THE TYMPANUM. G. CLAUS, Arch. f. Ohren-, Nasen- u. Kehlkopfh. **142**:186, 1936.

According to Claus, a typmpanic exudate is easily recognizable if the tympanic membrane is normal and thus readily permeable by light rays. The upper level of the fluid in the tympanum appears as a dark concave line, which moves as the position of the head changes. This line is missing only in the relatively rare cases in which the entire tympanum is filled with exudate. The second characteristic sign of secretory catarrh is the yellowish color of the tympanum. Contraction of the membrane, which is frequent, the author considers less important in the diagnosis of a tympanic exudate. The recognition of such an exudate becomes considerably more difficult if there are pathologic changes on the tympanic membrane. In cases in which the tympanic membrane is thickened, a normally invisible level of exudate often becomes visible after air has been introduced into the middle ear. In cases in which pathologic changes in the tympanic membrane make the recognition of an exudate impossible, thorough anamnesis is important. On moving the head forward and backward, patients with this condition often have a feeling of fluid in the ear. Intelligent persons often state this spontaneously and occasionally report that with the head in a certain position the hearing improves. Some complain of a feeling of pressure or of fulness in the ear. These symptoms indicate a tympanic exudate, especially if the patient has had a cold previous to the appearance of the aural symptoms. The author shows further that, though many patients reject paracentesis if they are free from pain, puncture of the tympanum is helpful not only diagnostically but therapeutically. He performs this puncture with a syringe of 1 cc. capacity and a cannula 62 mm. long and 0.6 mm. in diameter. The puncture is made, if possible, in the anterior lower quadrant, otherwise in the posterior lower quadrant. In five years the author resorted to puncture of the tympanum in 60 cases of tympanic exudate. The quantities of exudate varied between 5 and 44 cc., in most cases between 20 and 30 cc. The puncture was followed by inflation of the middle ear with air. In some cases a second puncture had to be made. Complete cure was effected in 53 cases; in the remaining 7, considerable improvement was obtained. The author does not resort to puncture at once but performs first the necessary therapeutic measures on the nose and the pharynx, applies heat to the ear and catheterizes the tubes or resorts to politzerization. If these measures do not produce the desired result, puncture of the tympanum is resorted to.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

PATHOLOGIC AND CLINICAL ASPECTS OF ACUTE MASTOIDITIS. F. ALTMANN, Monatschr. f. Ohrenh. **70**:1465 (Dec.) 1936.

It is Altmann's opinion that among the numerous factors which influence the course of acute otitis or of the resulting mastoiditis two are of especial significance, namely, the type of the pathogenic micro-organism and the anatomic structure of the mastoid. To be sure, such factors as age and sex may likewise be of influence. The author studied the various factors in 1,457 cases, in 98 of which both ears were operated on. An analysis of the cases according to the pathogenic organisms disclosed hemolytic streptococci in 66.2 per cent, Bacillus mucosus in 18.7 per cent, pneumococci in 10.9 per cent and various other organisms in 4.2 per cent. The paper is accompanied with tables which record the incidence of the different micro-organisms in the two sexes and in the different age groups. These tables indicate that hemolytic streptococci are relatively more frequent in nurslings and particularly in children and young persons than they are in older persons, whereas pneumococci are comparatively rare in young persons but become more frequent later. In discussing the incidence of the various micro-organisms in the two sexes, the author says that pneumococci show a slight predominance in male subjects. Further, he shows that the pneumatization of the mastoid process exerts

an influence on the development and the course of mastoiditis. He differentiates four types of pneumatization, one normal and three inhibited types. In more than half of the cases the mastoid processes showed good pneumatization, but since the course of acute otitis, and with it the tendency toward the development of mastoiditis, is greatly dependent on the anatomic structure of the mastoid process, the incidence of the various types of pneumatization in patients with mastoiditis permitted no conclusion regarding the frequency of the various types in normal persons. The author analyzes the material in regard to the number of days elapsing between the onset of the otitis and surgical attention, the relation between this time factor and the age and sex of the patient, as well as that between the time factor and the type of infecting organism. The incidence of complications is analyzed with regard to these different factors. The author stresses the high mortality and particularly the high incidence of meningitis in pneumococcic infections.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

OTOGENIC MENINGITIS DUE TO THE GREKOWITZ BACILLUS IN TWINS. A. HEINDL JR., Monatschr. f. Ohrenh. **70**:1511 (Dec.) 1936.

Grekowitz described a gram-negative rod of the hemoglobinophilic group, which he designated as Bacterium haemophilum mucosum and which he observed in 4 cases of suppurating meningitis and 1 case of pneumonia. In 4 of the cases acute otitis existed and in 1 the pus contained the aforementioned micro-organism. Heindl observed a case of bilateral otitis with meningitis caused by the Grekowitz bacillus in a 5 month old nursling. It was the more noteworthy because a twin sister of the patient had died of the same disorder six weeks previously. After a detailed report of the clinical history and of the necropsy, the author describes the results of the histologic examination of the temporal bones, which indicated otogenic meningitis, severe acute otitis media with involvement of the medullary spaces and suppurating labyrinthitis of both sides. The route of transmission could not be definitely identified, but it was considered possible (1) that the otitis by way of the fenestrae produced labyrinthitis, which in turn produced meningitis or (2) that the invasion of the meninges took place by way of the tegmen or the edge of the petrosa. According to the serial sections, either route was possible.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

DANGEROUS FOREIGN BODIES. E. WESSELY, Wien. klin. Wchnschr. **49**:1674 (Dec. 10) 1937.

Wessely describes 3 cases in which a needle was lodged in the bronchus and the procedures by which removal was accomplished. It is interesting to note that in every case the accident consisted in the aspiration through a pea shooter of a toy wool-tufted needle dart intended to be blown out through the tube.

In case 1 roentgenographic examination showed the needle in the trachea, above the bifurcation. With the patient under local anesthesia, the tip of the needle, which had stuck in the mucous membrane of the wall, was loosened by endoscopic manipulation. At that moment the patient, a boy, coughed the needle into the operator's eye!

In case 2 the roentgenogram showed the needle with the point embedded above the bifurcation. With the patient under local anesthesia, the tip of the needle, which the patient was under local anesthesia there was an attack of coughing, after which it was found that the point of the needle had penetrated the ring of the keel and showed against the lateral wall of the left principal bronchus, behind the aortic arch, while the tuft was in the right principal bronchus. First, it was necessary to push this wool fluff into the bronchus of the inferior lobe of the right lung. By thus moving the tuft the author opened up the lumen in the vicinity of the bifurcation to some extent, making room for removal of the needle into the right

principal bronchus. Then, by quick manipulation the point of the needle was brought into the end of the tube and withdrawal accomplished.

In case 3 the needle was located in the right principal bronchus. Bronchoscopic examination with the patient under local anesthesia showed that the bronchus was almost completely closed by the fluff on the end of the needle. The needle point was in the mucous membrane of the second ring, and it had also penetrated the wall. An attempt was made to push the needle deeper in order to free the embedded point, but without success. It became evident that the needle was wrapped in the wool and that the head was caught fast in the bronchus at a point between the middle and inferior lobes of the lung. By bending the end of a long probe, the author made a hook, and with this he grasped the needle from below. At the same time pressure was applied from above with pincers, and the needle was loosened and extracted without further difficulty.

None of the patients showed any subjective or objective signs of irritation during an observation period following each operation.

ABT, Chicago.

RELATION OF PNEUMATIZATION TO COURSE OF ACUTE OTITIS MEDIA. H. BARTH, Ztschr. f. Hals-, Nasen- u. Ohrenh. **41**:137, 1936.

This report by Barth is based on 717 cases of acute otitis media which were observed in his clinic in four years. Surgical treatment was resorted to in 510 of the cases, and conservative treatment was employed in the others. There were 20 (2.78 per cent) fatalities from otogenic complications. The author discusses the value of the roentgenogram, pointing out that it gives a good survey of the pneumatization. To be sure, in cases of acute otitis media it is often difficult to estimate the cellular structure (regular or irregular arrangement of cells). The author adopts Schwarz' classification of five different types of pneumatization. Acute otitis media may occur in association with all types, but it is most frequent when there is good development of the cells. In cases of considerable inhibition of pneumatization, acute otitis media often heals spontaneously, and surgical treatment is less often needed than when pneumatization is good. The duration of the process is usually greater in cases of spontaneous cure and inhibited pneumatization than in cases of good pneumatization. In patients with unilateral otitis media in whom the pneumatization was different on the two sides, the ear with the poorer pneumatization was somewhat more often diseased than the ear with the better developed cells. Among 13 patients with bilateral otitis media but varying pneumatization, there were 10 in whom the course was the same on both sides; in 3 cases antrotomy had to be done on the better pneumatized ear, whereas the other ear healed spontaneously. Subperiosteal abscesses were seen with all types of pneumatization, except those in which cell formation was no longer demonstrable. Contrary to expectation, subperiosteal abscesses were somewhat more frequent in children between the ages of 5 and 9 years than in those between 2 and 4 years. In the higher age groups subperiosteal abscess became somewhat less frequent. The better the pneumatization, the more frequent is the subperiosteal abscess. No relation between the sinal involvement and the degree of pneumatization could be detected except that when there was no pneumatization the sinus was relatively often involved. However, on account of the small number of cases, no general conclusions can be drawn. Complications like labyrinthitis, extradural abscess and nonlabyrinthogenic meningitis were observed chiefly in patients with good or normal pneumatization. In a surprisingly large number of cases influenzal otitis or infection with pneumococci or with Bacillus mucosus affected patients with normal pneumatization. Moreover, in the cases in which there was a fatal outcome, normal pneumatization predominated. However, although there are indications of relations between the anatomic structure of the mastoid process and the course of acute otitis media, there are so many deviations from this rule that in the individual case the prognosis cannot be based on the pneumatization.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

OTITIS IN INFANTS. A. TEN BOKKEL BUININK, Maandschr. v. kindergeneesk. **7**:91 (Dec.) 1937.

The author gives a summary of the different forms of otitis observed in infants in his clinic. He discusses the well known problem of the relation between otitis and feeding disturbances in infancy. Rarely otitis leads to chronic trouble. Latent mastoiditis may accompany acknowledged otitis but may also exist without any evident symptom in the ears. The author is of the opinion that in all cases of toxicosis in which no etiologic factor can be found, and in which there is no favorable reaction to the usual treatment, an antrotomy should be performed.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Lungs, Pleura and Mediastinum

TYPE-SPECIFIC ANTI-PNEUMOCOCCIC SERUM THERAPY. W. D. SUTLIFF, Illinois M. J. **72**:511 (Dec.) 1937.

Sutliff reviews the development and progress of type-specific antipneumococcic serum therapy. He finds that no therapy for pneumonia that is offered to physicians has been so thoroughly tested as antipneumococcus serum therapy. He advocates its more general use.

BARBOUR, Peoria, Ill.

A NEW SIMPLIFIED TECHNIQUE FOR THE DRAINAGE OF LUNG ABSCESS EMPLOYING GRADUATED TROCHARS. O. H. WANGENSTEEN, J. Thoracic Surg. **7**: 181, 1937.

Only when localization has occurred, should surgical intervention be contemplated.

The preliminary operation is done after a study of roentgenograms. Anesthesia is obtained with procaine hydrochloride. Segments from 5 to 8 cm. in length are removed from two adjacent ribs overlying the abscess, and the intercostal muscle bundle is excised. It is almost invariably necessary to use a gauze pack to assure firm agglutination between the visceral and the parietal pleura and to permit safe external drainage. A wisp of the gauze pack should be allowed to project through the muscle plane overlying the rib resection. The skin is closed with interrupted sutures.

The second stage of the operation is performed from five to seven days later, when the wound is reopened and the gauze removed. An aspirating needle is guided into the lung. Absence of resistance indicates that the cavity of the abscess has been reached, as may also coughing by the patient. For this stage Wangensteen has evolved a technic different from that in which a grooved director is pushed into the cavity beside the aspirating needle and enlargement of the tract made with a knife, scissors or the finger to permit evacuation of the abscess and external drainage. He uses a series of graduated trochars, each with a knifelike edge, aided with the coagulation current of the surgical diathermy apparatus. The track of the aspiration needle into the cavity can be followed by passing increasingly larger trochars over one another and applying the coagulating current in turn over each until a sufficiently large tunnel has been established to permit adequate drainage. Bloodless drainage of a pulmonary abscess may be quickly established in this manner, with minimal destruction of lung tissue.

HEAD, Chicago.

CYSTIC DISEASE OF THE LUNG. W. H. FIELD and L. ROSENBERG, J. Thoracic Surg. **7**:218, 1937.

A boy aged 6½ months was examined because of cough and dyspnea. At birth an abnormality in the contour of the chest had been noted, and a few days

later there was rapid and labored breathing. The heart was displaced to the left, and the entire right lung showed opacity. On thoracotomy a large amount of fluid was withdrawn from this lung. Partial collapse of the lung occurred. Because there was no improvement, operation was performed, which revealed a cyst in the upper half of the right lung. It had a spongy lining enclosing a greenish, mucoid and slightly foul collection of about 3 ounces (88 cc.) of pus. This was aspirated and the cavity washed out. At a second operation the lining of the cyst was scraped and the cavity lavaged with sterile water, a 25 per cent solution of silver nitrate and double strength saline solution. Recovery followed.

HEAD, Chicago.

ACUTE EMPYEMA IN CHILDREN: THE DURATION OF ILLNESS PRIOR TO TREATMENT A FACTOR IN MORTALITY RATE. G. S. BAKER, M. Clin. North America **21**:1367 (Sept.) 1937.

Patients rarely die from empyema but from such complications as septicemia, meningitis, abscess of the brain, pericarditis, pulmonary abscess and peritonitis. A frequent complication not to be overlooked is postoperative pneumonia in the contralateral lung. Horine and Baker believe that the outcome of empyema depends not so much on the type of infecting organism or the particular method of treatment used as on the duration of the illness prior to treatment. In their series a sharp line of demarcation was observed between fatal conditions and those from which the patients recovered between three and four weeks after the onset of the initial illness. Age is probably another important element in prognosis, since no death occurred in the children who were between 6 and 12 years of age.

It is not to be understood that the plea for early diagnosis is also an appeal for immediate operation but rather that early recognition of the condition makes possible prompt and adequate treatment based on the particular factors in each case.

EUGENE H. SMITH, Ogden, Utah.

MEDIASTINAL GANGLIO-NEUROBLASTOMA. F. D. HART, Proc. Roy. Soc. Med. **30**:1195 (Aug.) 1937.

This condition is reported in a boy aged 6 years. He was admitted to the hospital because of pain in the abdomen for one week and pain in both knees and in the left side of the face and small glands of the neck for four weeks. He had failed to gain weight for four months. Glands were palpable on both sides of the neck and in both axillas. A roentgenogram of the chest showed an oval mass behind the heart, alongside the vertebral column, in the posterior mediastinum. At first there was acute pain in the left hip and a few days later in the right hip. The tumor was removed with the patient under general anesthesia. The pathologist's report on the tumor was that it had a firm yellow "cortex" with a red, vascular "medulla."

Microscopically, the solid tissue consisted of a fibrillar matrix containing a number of pale rounded cells of varying sizes. The cells resembled nerve ganglion cells. The diagnosis was neuroblastoma arising in a ganglioneuroma. The report includes the results of a full physical and hematic examination and is accompanied by a roentgenogram of the chest. The operation is also described in some detail.

WILLIAMSON, New Orleans.

A CASE OF CONGENITAL CYSTIC DISEASE OF THE LUNG REMOVED BY OPERATION. T. HOLMES SELLORS, Tubercle **19**:65 (Nov.) 1937.

A girl of 18 years told of respiratory symptoms extending over a period of several years. The clinical and roentgenologic diagnosis was bronchiectasis

involving especially the left lung. The roentgenogram also showed a small curved opacity close to the midline on the left side, which on close inspection was seen to contain many saclike spaces containing contrasting fluid. At operation, two years later, a small dark mass was found deep in the chest, attached to the mediastinum, and this mass proved to be the lower lobe of the left lung. The upper lobe filled practically the whole of the pleural cavity and was of a healthy color and texture. The cystic lobe was removed. It was found to contain multiple cystic spaces lined with normal bronchial epithelium. It showed an entire absence of aerated alveolar tissue. The muscular and elastic tissue was hypertrophied, and there was an excess of mucous glands. Irregular fragments of cartilage were seen about the cysts. The bronchiectasis in the upper lobe was apparently acquired. The condition in the lower lobe appeared to have resulted from maldevelopment in the region of the small bronchi or bronchioles, with consequent failure of alveolar tissue to connect with the air tubes.

EUGENE H. SMITH, Ogden, Utah.

CLINICAL STUDY AND PATHOLOGIC ANATOMY OF BRONCHOPNEUMONIA IN SUCKLING BABIES. F. FELL, Pediatria **45**:226 (March) 1937.

In the majority of cases of acute bronchopneumonia in suckling babies the pneumococcus is the cause. When other organisms are found, they play a secondary part, being usually found in the respiratory tract. Schwarz recently proved by means of cultures and puncture of the pneumonic focus that the pneumococcus was present in all his cases and that it was associated with staphylococcus only once.

According to Fell, the type IV pneumococcus predominates in these cases. She cites Mya as stating that the frequency of bronchopneumonia in sucklings is due to the shortness of the bronchi, the absence of expectoration, the compression of the right lung and the constant supine position of the infant.

The season is of importance. March presents the highest incidence of the disease and September the lowest. From a study of the clinical charts it appears that bronchopneumonia is preceded by an infection of the upper part of the respiratory tract in 80 per cent of the cases.

Fell also noted that the fever follows an atypical course, that a febrile child with bronchopneumonia usually dies and that many of her patients showed dilatation of the alae nasi and cyanosis. Other concomitant signs of the disease are dyspnea, diarrhea, vomiting and aphonia.

As regards complications, empyema occurred in 8 cases, purulent arthritis in 1, subcutaneous mulitple abscesses in 20 and septicemia in 10. The pneumonic process was most frequently found localized in the inferior lobes of the lungs and less frequently in the middle lobe of the right lung and superior lobes.

However, according to Salmieri, the right lung, especially the superior lobe, and the inferior lobe of the left lung, are most frequently attacked.

The average duration of the disease is twenty-five days; the long course is due to the constant reinfection of the lungs and therefore the slow resolution. The slow resolution is due to a lesion of the lymphatic system that slows the absorption of pulmonary exudate.

In the 225 cases studied by Fell the mortality was 60 per cent. Precisely 68 per cent of the deaths occurred in the first six months of life, 32 per cent in the period from the sixth to the twelfth month and 18 per cent in the period from the twelfth to the twenty-third month.

She concludes by saying that the diagnosis of bronchopneumonia in sucklings is difficult because they do not always show physical signs, that dyspnea appears early and is usually accompanied by cyanosis and meteorism and that the disease should be differentiated from acute bronchitis and capillary bronchitis (she states emphatically that the latter is not a rare form of disease, as some would lead one to believe), and that pleurisy is frequent even in sucklings but not always detected clinically. In closing she states that the acute bronchopneumonia of the

suckling is a morbid process presenting a varied clinical picture and that only accurate investigation of all the symptoms can facilitate diagnosis and render the treatment efficacious.

PALMIERI, Brooklyn.

FIBROSIS IN THE BRONCHOPNEUMONIA OF SUCKLINGS. G. BETTINARDI, Pediatria **45**:304 (April) 1937.

Pulmonary fibrosis is a frequent finding in bronchopneumonia in sucklings. The author excludes from consideration all other forms of bronchopneumonia, whether of lobar type, of tuberculous or syphilitic type or due to a cardiovascular process. He limits himself in the study to these fibrotic processes: acute, subacute and chronic.

He confutes the claims of writers who assert that this type of bronchopneumonia is the indurative or interstitial type. From the histologic point of view pulmonary fibrosis is due to an increase of connective tissue obliterating alveoli and giving to the tissue, which is smooth and brilliant, an increased density, with disappearance of the characteristic crepitation on squeezing.

Of 720 cases studied, 34 were reported because in these the histories were complete, including autopsies. Twelve patients gave a history of an infection of the upper part of the respiratory tract; 4 had measles; 5 had bronchitis; 2 had pertussis; 1 had pertussis and bronchopneumonia, and 1 had bronchopneumonia ten months before.

It is a matter of fact that pneumonic processes accompanied by a peribronchial diffusion, especially the bronchopneumonia secondary to pertussis or to measles, are the ones that contribute most to the fibrosis. These processes are not always due to streptococci; at times one encounters pneumococci. Two possible reasons why bronchopneumonia of this type does not resolve are: 1. An inflammatory process occludes the lymphatic system. 2. There is lack or absence of proteolytic ferment in the leukocytes of the exudate. Other causes that contribute to pulmonary fibrosis are a circulatory disturbance or some cause that favors collapse of the alveoli.

It is believed that the production of connective tissue comes from the polyblasts. As to localization, both lungs are affected equally, especially the inferior lobes.

Bettinardi concludes by saying that pulmonary fibrosis can be found in chronic pneumonia whether this is indurative or interstitial, that pulmonary fibrosis cannot exist without a proliferation of connective tissue that obliterates alveoli, that pneumococci are frequently found, especially in infants older than 5 months, that clinical diagnosis is practically impossible but that occasionally roentgenograms help in diagnosing the condition, and that patients with pulmonary fibrosis get well clinically but not anatomically.

PALMIERI, Brooklyn.

PNEUMONIA IN EARLY INFANCY. C. GIANELLI, Arch. de pediat. d. Uruguay **8**:676 (Nov.) 1937.

Gianelli reports the results of an extensive study of 136 cases of pneumonia over a period of three years. The physical signs were clear on the fifth day in 80 per cent of the cases. All of the patients showed a negative reaction to tuberculin. Roentgen signs persisted long after the crisis had developed.

SCHLUTZ, Chicago.

PULMONARY ATELECTASIS DUE TO A FOREIGN BODY. A. INVALDI and R. PUIG, Rev. Soc. de pediat. de Rosario **2**:211 (Oct.) 1937.

Following a roentgen examination a 6 year old child was thought to have pulmonary atelectasis of unknown origin. Tests for tuberculosis were negative. In a fit of coughing and vomiting the child expelled a transparent foreign body.

SANFORD, Chicago.

THE VEGETATIVE NERVOUS SYSTEM IN LOBAR PNEUMONIA AND THE EFFECT OF DRY CUPPING. P. A. PONOMAREVA, Pediatriya, 1937, p. 38.

In the acute stage of lobar pneumonia there is irritability of the vegetative nervous system. After the crisis, a predominance of function of the parasympathetic nervous system ensues. The administration of epinephrine causes an active reaction before the crisis; there is accentuation of the vagotonia after the crisis. Experiments with epinephrine and atropine may determine the approaching crisis. Dry cupping has no influence on the deranged functions.

SEMENENKO-MCKHANN, Boston.

INTRODUCTION OF ROENTGEN CONTRAST MEDIUMS INTO THE LUNGS BY INHALATION. E. K. AHVENAINEN, Acta pædiat. **21**:1, 1937.

This investigator was no more successful in his efforts to visualize the bronchial tree through the inhalation of vaporized opaque material than others have been who have experimented with the same technic. Irrespective of whether the solvent was aqueous or oily, the shadows were diffuse and hazy, and the outline of the bronchial tree could not be identified satisfactorily. The experiments were confined to guinea pigs.

MCCUNE, New York.

THE STRUCTURE OF THE LUNGS OF PREMATURELY BORN AND FULL TERM INFANTS, WITH PARTICULAR ATTENTION TO THE DEVELOPMENT OF THE ELASTIC FIBERS AND THE CAPILLARIES. E. KLEMOLA, Acta pædiat. **21**:236, 1937.

This is a preliminary report of an investigation of the histologic features of the lungs of premature and full term infants. It is well illustrated and documented. The stage of development of the elastic structures of the lungs is positively correlated with the weight of the infant. For this reason the respiratory activity of the premature infant, at least during the first two weeks of life, is handicapped by anatomic peculiarities; these are promptly compensated for by rapid growth of the elastic structures, with the result that within a month or two the lung of the premature infant may appear more mature than that of the full term infant from the point of view of elastic fibers. A positive correlation also exists between the density of the network of pulmonary capillaries and the weight of the newly born infant.

MCCUNE, New York.

COLLAPSE OF THE LUNG OR CONGENITAL MALFORMATION. G. G. HUËT, Maandschr. v. kindergeneesk. **7**:113 (Dec.) 1937.

Huët describes the case of a girl of 4 years who showed some symptoms of collapse of the lung. A thorough examination disclosed, however, the existence of a congenital malformation, namely, a small left lung. Huët considers the problems concerning congenital malformation of the lungs.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

SURGICAL SIGNIFICANCE OF MELENA IN CHILDHOOD. W. E. LADD, New England J. Med. **217**:649 (Oct. 21) 1937.

Conditions or diseases causing melena in children are, in the order of their surgical interest, intussusception, Meckel's diverticulum, intestinal duplications, polyps, idiopathic ulcerative colitis, hemorrhagic disease of the newborn, purpura, splenomegaly with hematemesis, anal fissure, foreign body and certain other rare diseases.

The best treatment of intussusception is surgical. From 1908 to 1936, 434 patients with this condition have been treated at the Children's Hospital, Boston.

with better and better results. In the last eight years no death has occurred in any patient who was received at the hospital within thirty-six hours after the onset of symptoms. The factors in this improvement of results in order of importance are: (1) earlier diagnosis, (2) improved surgical technic and (3) better preoperative and postoperative care.

When a presumptive diagnosis of Meckel's diverticulum has been made, operation should be resorted to at once, so as to avoid the serious complications that accompany delay.

The polyp, if located in its commonest place, a few centimeters inside the anus, can easily be removed by transfixing the pedicle and excising with the actual or the electric cautery.

Idiopathic ulcerative colitis is one of the inflammatory conditions which have a surgical implication. Ileostomy has proved a life-saving procedure in many instances.

In idiopathic purpura (thrombopenic purpura) the preferred treatment is by transfusion, splenectomy or both.

In splenomegaly with hematemesis and melena splenectomy alone has not provided an effective remedy.

Blood in the stools caused by swallowing a foreign body must always be thought of—the open safety pin is the foreign body most frequently found.

Among the rarer conditions which have melena as a symptom are tuberculosis, the granulomas and sarcoid, the latter often described under the confusing title of "regional ileitis."

GENGENBACH, Denver.

CONGENITAL MICROCOLON. J. R. ABDALA and others, Arch. argent. de pediat. **8**:1281 (Dec.) 1937.

The authors report the case of a newborn infant who passed no meconium for twenty-four hours and later vomited fecal material. A rectal tube reached only 12 cm. with difficulty. Laparotomy showed a microcolon. The baby died four hours after birth.

The authors review the various theories as to the causes and genesis of such an abnormality.

SCHLUTZ, Chicago.

TREATMENT OF FERMENTATIVE DIARRHEA AND DYSPEPSIA IN INFANTS. V. ZERBINO, Arch. de pediat. d. Uruguay **8**:693 (Nov.) 1937.

Zerbino suggests the use of egg white, diluted with water and added to cow's milk, in the treatment of fermentative diarrhea and dyspepsia in infants. To the egg white, 250 cc. of freshly boiled water is added and gently stirred. Another 250 cc. is then added and the mixture filtered. This mixture is used for diluting milk. Sugar or flour may be added to the extent of 2 per cent. The author claims good results from this milk mixture but warns against its use in allergic infants.

SCHLUTZ, Chicago.

ILEUS DUE TO FOREIGN BODY FOLLOWING APPENDECTOMY. G. LOEWE, Beitr. z. klin. Chir. **163**:384, 1936.

Loewe reviews the case of a 12 year old boy from whose small bowel a piece of gauze was removed three months after appendectomy.

RUBIN, Boston.

CLOACAL MALFORMATION WITH CONGENITAL REDUPLICATION OF THE CECUM AND APPENDIX. C. H. SCHRÖDER, Beitr. z. klin. Chir. **163**:481, 1936.

A 4½ year old boy was found to have malformation of the cloaca—the large bowel was anastomosed to the bladder, and the cecum and appendix were double. The large bowel was abnormally short and showed no differentiation of ascending,

transverse or descending colon. Other anomalies present were spina bifida and asymmetry of the sacrum. The embryologic aspects are considered in detail.

RUBIN, Boston.

DIAGNOSIS AND TREATMENT OF PNEUMOCOCCIC PERITONITIS IN CHILDREN. V. I. APOSTOL and Y. M. VOLOSHIN, Vrach. delo **19**:887 (Dec.) 1937.

Apostol and Voloshin point out the difficulties in diagnosis of pneumococcic peritonitis in infants and young children, which is confused with the toxic states which so frequently accompany acute gastrointestinal disturbances in such subjects. The frequency of pneumococcic peritonitis in children as compared with other types of peritonitis is pointed out. The various manifestations of the disease and the forms of therapy for it are dealt with and illustrated by reports of 5 cases. Attention is called to the controversy in regard to the treatment of pneumococcic peritonitis. The authors' views on the subject are as follows: 1. The patient with pneumococcic peritonitis should be under close surgical observation as soon as the diagnosis is established. 2. Diagnostic abdominal punctures should be abandoned, as they contribute greatly to the development of complications. 3. Operative procedures should be resorted to only in the third stage of the disease, namely, when a definite localization of the process takes place. 4. A simple laparotomy is the operative method of choice. 5. The after-treatment of the wound should be: infrequent dressing, application of tampons saturated with cod liver oil and local use of heat.

The authors have had no experience with the use of specific serotherapy in pneumococcic peritonitis.

BODER, Los Angeles, Calif.

THE BLOOD PICTURE, ERYTHROCYTE SEDIMENTATION RATE AND UROBILIN METABOLISM IN PERIODIC KETONURIC VOMITING, TOGETHER WITH A DISCUSSION OF THE ROLE OF INFECTION IN PRECIPITATING THE ATTACKS. J. STRÖM, Acta pædiat. **20**:131, 1937.

The implications of the title are fulfilled in a somewhat discursive fashion. The article is based on the author's experience with 11 children during nine spontaneous attacks of vomiting and during four attacks provoked intentionally by dietary measures.

The white blood cell count was found to be normal between attacks. The most characteristic alteration during bouts of vomiting was an increase of polymorphonuclear elements, associated with the appearance of immature myeloid cells in the blood; during episodes of mild or of moderate severity this increase was usually compensated for by lymphopenia, with the result that no increase of the total leukocyte count occurred. During severe attacks the total white blood cell count was apt to rise sharply, although values above 20,000 per cubic millimeter were exceptional. A good degree of correlation was found to exist between the total leukocyte count and the sedimentation rate of the erythrocytes: the latter was only slightly increased in mild attacks but more strikingly accelerated in severe episodes. It returned to normal more slowly than the white cell count. Studies of the urinary excretion of urobilin in 9 cases demonstrated that the output was diminished during the bout but increased conspicuously during a period of approximately four days immediately after the attack. The author ascribes the the changes in the white blood cell count and sedimentation rate to noninfectional metabolic influences. He urges that the role of infection in the genesis of cyclic vomiting has been overemphasized, although he concedes freely that the occurrence of infection may precipitate the onset of the attacks in individual instances. He relates the alterations in excretion of urobilin to hepatic damage and to derangement of intestinal function, which he has previously shown to accompany attacks of recurrent ketonuric vomiting. A discussion of the differential diagnosis of cyclic vomiting is provided, and an extensive bibliography is appended.

MCCUNE, New York.

Nervous Diseases

LESIONS OF LEAD ENCEPHALITIS IN CHILDREN. S. S. BLACKMAN JR., Bull. Johns Hopkins Hosp. **61**:1 (July) 1937.

This is a careful and complete clinical and pathologic study of 22 cases of lead encephalitis in children. The literature is reviewed, and there is a good bibliography.

Lesions were found through the entire nervous system but most abundantly in the cerebral hemispheres and cerebellum.

The microscopic changes were those of a serous inflammation. Vascular lesions were found, including capillary necrosis and thrombi, together with abundant exudate, damage of tissues and evidence of repair. Most of the injury to the nerve tissue seemed dependent on accumulation of exudate.

The exudate was composed of serous fluid, usually without fibrin. A part was coagulated in the brain by the solution of formaldehyde used in fixation; some was older, inspissated in appearance, and was coagulated in the tissue before death; a portion was extracted by the fixing and dehydrating agents.

The author is impressed with the fact that the signs of encephalitis appeared during the hot months of summer and fall in 19 of the 22 cases. He suggests that factors which cause vasodilatation, such as fever and the summer temperatures, may be important in precipitating the lesions in the brain. Experimental evidence is cited in support of this idea.

LYTTLE, New York.

CEREBRAL THROMBOSIS CAUSING DELETION OF ARTIFICIAL WRITING CENTER IN LEFT CEREBRAL HEMISPHERE OF LEFT-HANDED MAN. J. M. NIELSEN, Bull. Los Angeles Neurol. Soc. **2**:176 (Dec.) 1937.

Nielsen reports the case of a man who was "born left-handed," was forced to write exclusively with his right hand in school and had never written with the left hand since the age of 8 years. At the age of 68, while suffering from severe arterial hypertension and arteriosclerosis, he had left hemiplegia with complete motor and sensory aphasia. The aphasia lasted twenty-four hours and the hemiplegia three weeks. Seven months later he awoke with right hemiplegia, which left the right hand sufficiently free for attempts at writing. He then had agraphia with the right hand, being unable to write a single letter with that hand, though he could write numbers to dictation. Ability to write with the left hand was preserved, but he could not copy with the right hand what he had written with the left. He could read without difficulty, cut with scissors held in the left hand and draw pictures with either hand. Mental calculation was impaired. Three days later the hemiplegia had greatly diminished, but it was not until the twelfth day that he could again write with the right hand.

Nielsen believes that the patient had two "writing centers," one on each side of the brain, but that the center for general knowledge of language remained in the right hemisphere, with connections between the two centers through the corpus callosum. Recovery from the aphasia associated with the first (left) hemiplegia could not have been due to substitution of the left center for the right but must have resulted from restoration of the function of the right center, since the subsequent right hemiplegia produced only agraphia, not total aphasia. The "writing center" in the left hemisphere was "artificial," and at the time of the second, or right, hemiplegia, it was separated by the lesion from the language area on the right side of the brain.

MACKAY, Chicago. [ARCH. NEUROL. & PSYCHIAT.]

THE EPILEPTIC SCHOOL CHILD (HOW MAY WE UNDERSTAND AND TREAT HIM?). F. L. PATRY, New York State J. Med. **37**:1553 (Sept. 15) 1937.

In order to learn the present day practice regarding epileptic school children a questionnaire was sent to 40 school physicians in the state of New York. Nineteen replied. A study of these answers shows that the attitude toward the

epileptic children has changed. Ten years ago there was a tendency to exclude all of these children from regular grades. Today, if an epileptic child does not have severe attacks or present too much difficulty in handling, it is considered wise to keep him in school. Much also depends on the intellectual ability of the child. If the intelligence quotient is below 65, there is a tendency to exclude him. The school physician and nurses cooperate with the family physician to secure proper diagnosis and treatment, and teachers are instructed regarding management of seizures. If the child does not have severe attacks and there are no highly emotional children in the grade, the seizures do not cause undue disturbance. Children too ill to attend school receive assistance through the Bureau for Handicapped Children of the New York state department of education.

AIKMAN, Rochester, N. Y.

NON-PARASITIC EXTRADURAL CYST OF THE SPINAL CANAL. THOMAS S. B. KELLY, Lancet **2**:13 (July 3) 1937.

Kelly reviews the 11 cases of this condition on record and adds the case of a boy aged 15 who showed marked motor weakness of the lower extremities, moderate sensory impairment and roentgen evidence of enlargement of the spinal canal, with thinning of the pedicles. The origin of nonparasitic extradural cysts seems to be "an arachnoidal prolongation around the posterior root, herniating backwards through a congenital defect, as a finger-like process." The patient was operated on and made a complete recovery.

KRINSKY, Boston. [ARCH. NEUROL. & PSYCHIAT.]

PACHYMENINGITIS HAEMORRHAGICA. R. P. BERINGER, Infancia **1**:16, 1937.

Beringer reports a single case of hemorrhagic pachymeningitis with complete recovery. He considers the case in detail.

HERRON, Monroe, La.

SEROTHERAPY OF CEREBROSPINAL MENINGITIS. H. D. GONZALEZ and C. FLORIANI, An. Fac. de cien. méd de La Plata **1**:397, 1937.

The authors describe briefly the methods of obtaining antimeningococcus serum, stressing that the strains of meningococci existing in their country differ from those of Europe and North America and emphasizing that serum from the latter continents is not as efficacious as serum produced by the National Department of Hygiene. (Their experience in this respect parallels that of most epidemiologists in this country.) After enumerating the various avenues by which antimeningococcus serum may be administered, Gonzalez and Floriani describe the technic employed by Professor Destéfano, which was adopted as a routine practice in the treatment of 57 patients. In cases in which the patient is seen within twenty-four hours after the onset of symptoms, this technic consists in the administraiton of 100 cc. of serum daily for four consecutive days. If the entire amount cannot be given intraspinally, the remaining amount is introduced intramuscularly. If, however, 100 cc. can readily be administered intraspinally, an additional 50 cc. is given intramuscularly. Their experience has been that in the majority of cases in which the patient is treated early a single series of four daily injections suffices. In cases in which the onset has preceded treatment by forty-eight hours, three days' interval is allowed to lapse after the initial series of four injections, and then if the spinal fluid is turbid another series of four injections is instituted. In cases in which the disease has been of more than forty-eight hours' duration, the three day interval of freedom from injections is modified so that an additional consecutive day of treatment is added to the customary four day series for each thirty-six hours past the arbitrary forty-eight hours which is didactically set by the authors as demarcating an "ordinary" from a "tardy" case.

To the reviewer, this treatment appears to be largely of historical interest. The authors seem not to take into account the cytologic, chemical or bacteriologic character of the spinal fluid in determining the necessity for additional serotherapy, being guided apparently solely by the turbidity. The total quantity of serum administered seems excessive in the light of experience in the United States, but a difference in the antibacterial qualities of the serum used by them may account for the apparent discrepancy. KALISKI, San Antonio, Texas.

A CASE OF MARFAN'S DISEASE. A. GAREISO, Arch. de pediat. d. Uruguay **8**:669 (Nov.) 1937.

Gareiso reports this condition in a 13 year old girl. She showed neuropsychic disturbances progressing to dementia. She also had spastic paraplegia and manifestations of pyramidal lesions. The Wassermann reaction of the blood and that of the spinal fluid were positive. The spinal fluid showed lymphocytosis, and the test for globulin and the Lange colloidal gold test were positive. The author believes this to have been a typical case of Marfan's disease.

SCHLUTZ, Chicago.

DISEQUILIBRIUM OF THE VEGETATIVE NERVOUS SYSTEM. C. M. BARBEROUSSE and D. BARBATO, Arch. de pediat. d. Uruguay **8**:705 (Nov.) 1937.

The authors present the case of a patient with disequilibrium of the vegetative nervous system. This patient had shown intense dermographia since the age of 5 years. There was no history of allergy. The patient had mild signs of vagotony and hyperthyroidism. The treatment for these conditions had no effect on the dermographia.

SCHLUTZ, Chicago.

PARALYTIC CHOREA (SYDENHAM). A. DUTRUEL and O. E. USINGER, Rev. Soc. de pediat. de Rosario **2**:228 (Oct.) 1937.

The treatment for paralytic chorea is by arsenic, given internally, and by the faradic current. The prognosis is good.

SANFORD, Chicago.

A SOLITARY TUBERCLE IN THE PONS OF A NURSLING. H. PETER, Monatschr. f. Kinderh. **71**:316 (Dec.) 1937.

Peter reports a case of solitary tubercle in the pons, with the observations at autopsy. The child had pulmonary tuberculosis and symptoms of an involvement of the central nervous system, starting with paralysis of the external rectus muscle of the eye, followed by paralysis of the facial nerve. An unusual feature of the case was that the neurologic symptoms followed a fall. A fracture of the skull was suspected at first.

GERSTLEY, Chicago.

EPIDEMIC ENCEPHALITIS IN PATIENTS WHO HAVE HAD POLIOMYELITIS. W. KLIMKE, München. med. Wchnschr. **84**:1413 (Sept. 3) 1937.

The question has been asked whether a person who has had acute anterior poliomyelitis is more likely to contract epidemic encephalitis than a person who has been in good health. Some patients who had had poliomyelitis presented epidemic encephalitis fifteen or twenty years later. Anatomically both diseases are nonsuppurative encephalitides or encephalomyelitides. However, they are usually different in the localization of the lesions and in the character of the cellular reaction. In addition, the difference in the symptomatologic picture indicates that the two diseases are clinical entities. After considering all the factors involved, Klimke concludes that a person who has had poliomyelitis is not more susceptible to encephalitis than a person who has not had that disease.

BRAHDY, Mount Vernon, N. Y.

SPASMUS NUTANS. G. OSTERBERG, Acta ophth. **15**:457, 1937.

Spasmus nutans is an infantile disease, usually beginning at the age of from 6 to 12 months but never after the third year. The classic signs are nystagmus of the head, torticollis and nystagmus of one or of both eyes. These signs disappear during sleep. The ocular nystagmus is intensified if the head is held still. Complete recovery occurs after about two years. Nystagmus of the head alone may occur and is suggestive of spasmus nutans, while if ocular nystagmus is the only sign present, as it may be, care must be taken to differentiate the condition from congenital or early acquired amblyopia associated with strabismus or refractive anomalies. Labyrinthine disease must be excluded by functional tests. The author gives short reports of 4 true and of 2 spurious cases of spasmus nutans.

PERKINS, New York. [ARCH. OPHTH.]

FETAL MICROCEPHALY DUE TO ROENTGEN IRRADIATION OF THE PREGNANT MOTHER. M. HIRVENSALO, Acta pædiat. **21**:188, 1937.

In 1926 Zappert drew attention to the possibility that roentgen irradiation of the pregnant woman during the early months of pregnancy may exert a seriously harmful effect on the fetus. In a critical examination of the published reports of 20 cases he reached the conclusion that the injury consisted essentially in an arrest of development at the stage to which it had progressed at the time of exposure to the roentgen ray. He regarded three stigmas to be characteristic of the damage produced by this agent: microcephaly, mental defect and gross deformities of the eyes. Statistical examination revealed that almost 50 per cent of fetuses that received roentgen radiation in the early months of gestation exhibited evidence of injury if they remained viable and survived to term. Zappert's "roentgenous fetal microcephaly" crystallized the implications of a considerable number of antecedent clinical and experimental observations; the correctness of his concept has been confirmed and the extent of the application of this concept amplified by several subsequent publications. It is now widely held that therapeutic and even diagnostic exposure of the mother's reproductive apparatus to roentgen radiation may injure the fetus in about 50 per cent of the cases; irradiation of extragenital parts is also under suspicion of producing harm. Exact information is not available concerning the quantitative aspects of the roentgen dosage; however, experimental evidence suggests that as little as 3 or 4 erythema doses may produce damage to embryonal nerve tissue. Less is known concerning the harmful potentialities of radium. Those who regard the possibility of damage to the fetus as real urge that roentgen irradiation for any purpose be used sparingly during pregnancy and that if any considerable amount of roentgen radiation is applied to the mother pregnancy should be terminated in order to avoid responsibility for the birth of a seriously defective infant.

The illustrative case reported possesses small value as evidence. The bibliography contains useful titles.

MCCUNE, New York.

Psychology and Psychiatry

INCIDENCE OF PILONIDAL SINUSES IN MENTAL DEFECTIVES. W. J. JOHNSON and A. G. LIVINGSTON, J. Nerv. & Ment. Dis. **87**:156 (Feb.) 1938.

One thousand mentally deficient persons varying in age from 1 to 40 years, residing in an institution for feebleminded persons, were studied to determine the incidence of pilonidal cysts. Only those showing genuine cysts were included. Thirty-four such persons were found (3.4 per cent); 20 were males, and 10 were females. Most of these persons showed other physical stigmas. None had had tuberculosis; 2 presented positive serologic deviations.

The pilonidal sinuses had caused these patients no discomfort and had at no time required treatment.

JAHR, Omaha.

SEX-LINKED MICROPHTHALMIA SOMETIMES ASSOCIATED WITH MENTAL DEFICIENCY. J. A. FRASER ROBERTS, Brit. M. J. **2**:1213 (Dec. 18) 1937.

A family group is described in which microphthalmia is inherited as a sex-linked recessive condition. The eyes in 6 affected members of this family show much variation in appearance. The blind males may be of normal mentality or may exhibit any grade of mental deficiency from feeblemindedness to profound idiocy. There is no mental deficiency in the family group apart from the blindness.

ROYSTER, University, Va.

PSYCHOSENSORIAL DEVELOPMENT OF INFANTS. T. SLECH, An. Soc. de peuricultura de Buenos Aires **3**:99 (April-June) 1937.

Slech gives a few tests which an infant should be able to carry out, as raising the head and following light with the eyes, and cites the value of such tests in the development of the normal infant. HERRON, Monroe, La.

INFANTILE FEEBLEMINDEDNESS. T. HELLER, Med. Klin. **34**:149 (Feb. 4) 1938.

Heller regards faulty gestation as the most important cause of feeblemindedness. The concept and the classification of feeblemindedness are vague. Children with severe feeblemindedness have a short life expectancy. Idiots and imbeciles are of importance mainly as regards care and institutionalization. Children with borderline feeblemindedness are differentiated with difficulty from children who are poorly trained or suffering from poor environment. Proper training of feebleminded children during the early years of life is important. Special kindergartens are desirable. Even in more advanced schools vocational guidance is more important than education. Many feebleminded persons can be useful in industry and agriculture.

Except in cases of hypothyroidism, endocrine therapy is of no avail.

SIEMSEN, Chicago.

CHILDHOOD FEARS. H. KRAMPFLITSCHECK, Ztschr. f. Kinderpsychiat. **5**:11 (May) 1938.

Fear is a biologic mechanism utilized in all living things for the preservation of life. In the infant total lack of fear must be considered a symptom of physical or mental inadequacy. On the other hand, exaggeration of fear, particularly in the older child, must be looked on as an emotional distortion of a normal psychologic attribute. In order to understand the significance of this distortion it is necessary to evaluate all factors that enter into its causation. The child must be investigated to determine his physical equipment, his mental makeup, his scholastic achievements, his social standing with his fellows, his domestic problems and everything else to which he is expected to react. Night terrors are considered from the point of view of their psychobiologic significance. JAHR, Omaha.

INCIDENCE AND CAUSES OF MONGOLIAN IDIOCY AS JUDGED BY CLINICAL EVIDENCE COLLECTED IN FINLAND. S. LAHDENSUU, Acta pædiat. **21**:256, 1937.

Mongolian idiocy occurs in Finland with about the same frequency as in other countries. The sexes are affected equally. In a survey of 250 cases the mean age of the living children was found to be 6½ years. In about half of those who died death occurred under the third year of age; pneumonia was the cause of death in about 50 per cent of those who died.

In this survey no evidence was uncovered to suggest that tuberculosis, syphilis, complications of pregnancy or endocrine disorders contributed to the production of mongolism. The average age of mothers of defective children at the time of birth of these children was found to be slightly higher than the average maternal age at the time of birth of normal members of the population. The

difference was so small from a statistical point of view that the author concludes confidently that advanced maternal age at the time of conception of the defective child plays a much less important role in the genesis of mongolism than has been generally ascribed to it. Furthermore, against the hypothesis that the child with mongolism is an "exhaustion product" is the fact that 28.3 per cent of the patients dealt with in this study were first-born infants; also, the additional fact that no difference could be demonstrated in the incidence of mongolism in large and in small families.

One of the striking findings in this series was the large incidence of mongolism in families characterized by mental disease, constitutional inferiority, congenital anomalies and other hereditary variations. For example, a twice married mother gave birth to 2 children with mongolism, each by a different father; each of 3 patients had a cousin with mongolism; one of a pair of binovular twins showed mongolism, while the other was normal.

The foregoing evidence points clearly to the hereditary character of mongolism; further evidence is found in studies of the occurrence of mongolism in twins: reports of 74 cases have appeared in the literature in which one or both of twins showed mongolism. It is highly significant that with a single exception all cases of mongolism in *one* of twins concerned twins of double ovum origin; whereas, in all cases in which both twins presented mongolism the twins were shown to be of single ovum origin.

The author supplies a useful synopsis of the criteria for distinguishing between uniovular and binovular twins; he also gives a helpful bibliography.

McCUNE, New York.

Diseases of the Genitourinary Tract

RENAL EXCRETION OF SULFANILAMIDE. E. K. MARSHALL JR., KENDALL EMERSON JR. and W. C. CUTTING, J. Pharmacol. & Exper. Therap. **61**:191 (Oct.) 1937.

The authors compare the excretion of sulfanilamide in the urine of dogs with that of creatinine, the latter being taken as a measure of the glomerular filtration rate. They conclude that the clearance of sulfanilamide is from 20 to 30 per cent of the simultaneously determined clearance of creatinine. The clearance of sulfanilamide is independent of the plasma level. It increases with increase in the rate of urine flow.

PILCHER, Cleveland.

INDICATIONS FOR THE USE OF AMMONIUM MANDELATE IN PYURIA IN CHILDREN. W. E. WHEELER, New England J. Med. **217**:643 (Oct. 21) 1937.

Patients with acute or recurrent pyelonephritis are usually encountered by the physician when they are in the febrile state, and at this stage it is well to treat them as sick persons and defer investigative procedures until after the temperature has fallen.

Culture of catheterized urine and identification of the infecting organism are important.

The phenolsulfonphthalein excreting power of the kidneys or the urea clearance is obtained as a routine in every case; also, the blood nonprotein nitrogen is determined and the concentration test is made.

For the intravenous pyelogram diodrast is injected intravenously with the patient in a moderate Trendelenburg position on the x-ray table, and roentgenograms of the region of the kidney and bladder are taken five, fifteen and thirty minutes after the injection.

The ammonium mandelate is given in the form of a 10 per cent elixir.

Over a period of eighteen months 51 children with acute, chronic or recurrent infection of the urinary tract were treated with mandelic acid salts. Of these, 39 (76 per cent) became free from their urinary infection.

Quite a few patients definitely require surgical intervention.

GENGENBACH, Denver.

RENAL RICKETS. S. VAN CREVELD, Rev. franç. de pédiat. **13**:229, 1937.

Van Creveld considers present knowledge of renal rickets and gives an excellent review of the literature. He particularly points out that the differentiation between renal rickets and primary hyperparathyroidism is sometimes difficult and that a careful analysis of the history is essential. In renal rickets renal symptoms may be found to predate the bony changes. He also considers the possibility of the whole picture of renal rickets being due to endocrine disturbance as proposed by Chown, although he does not think that such an etiologic explanation has been definitely established.

LESLIE, Evanston, Ill.

TREATMENT OF UNDESCENDED TESTES. E. A. TRAVELLA, Rev. Soc. de pediat. de Rosario **2**:222 (Oct.) 1937.

The treatment consisted in the intramuscular injection of from 250 to 3,000 international units of an androgenic substance (testosterone). It was successful in 10 boys from 3 to 14 years of age.

SANFORD, Chicago.

TORSION OF THE CORD IN CASES OF CRYPTORCHIDISM. L. JÓSA, Beitr. z. klin. Chir. **163**:45, 1936.

Severe forms of this condition are infrequent. Mild forms usually correct themselves easily. Correction occurs spontaneously more often when the testicle is in the inguinal canal than when it is in the scrotum.

The author reviews in complete detail 12 cases observed by others and a case which he observed.

The characteristic symptom is severe abdominal pain of several days' duration. A correct preoperative diagnosis was made in 4 of the cases discussed.

The greatest number of cases (6) occurred in testicles with tumor formation (carcinoma and sarcoma)—heaviness produces susceptibility to torsion.

The amount of degeneration of the testicle depends on the duration of the torsion.

RUBIN, Boston.

SECONDARY DISTURBANCES OF PORPHYRIN METABOLISM. J. BRUGSCH, Ergebn. d. inn. Med. u. Kinderh. **51**:86, 1936.

There are four types of pathologic porphyrinuria, which are distinguishable through determinations of the excretion of porphyrin in the urine, stool and bile:

1. Porphyrinuria associated with increase in enteral porphyrin. Porphyrin in the intestine arises as a result of abnormal putrefaction and bacterial synergy. Occasionally a rise is associated with ileus, when the subject is on a porphyrinogenic diet, as well as with gastric and intestinal bleeding.

2. Porphyrinuria resulting purely from increase in the endogenous formation of porphyrin. The increase may result from (*a*) disturbances in the metabolism of blood pigment, (*b*) central regulatory activities, (*c*) the action of toxins and (*d*) the breakdown of porphyrin-containing tissues. In these cases the increase in porphyrin is seen in the urine, stool and blood but not in the serum and is observed even when the diet is poor in porphyrin.

3. Porphyrinuria resulting from disturbances in the excretion of porphyrin by the liver cells. This occurs in a subject who is on a porphyrin-poor diet and is demonstrated by a drop in the porphyrin excreted in the stool and a simultaneous increase in that excreted in the urine. In these cases the biliary porphyrin is spilled over into the blood and blood serum. When the excretion of biliary porphyrin is entirely stopped in the liver cells, it can be demonstrated quantitatively in the urine. Here, also, there will be observed a rise in the urinary and fecal porphyrin when porphyrin building material is administered by mouth.

4. Porphyrinuria resulting from disturbances in the assimilation and excretion of exogenous porphyrin and porphyrinogenic substances (amines). This condition

arises chiefly when the subject is on a porphyrin-rich diet and when there is no increased formation of stercoporphyrin as a result of disturbance of the liver cells, in the sense of an inability to assimilate and excrete the resorbed porphyrin.

CAPPER, Philadelphia.

RENAL INFANTILISM. W. MALZ, Monatschr. f. Kinderh. **71**:305 (Dec.) 1937.

This is a case report with a photograph and a roentgenogram of a child whose illness was diagnosed as renal infantilism. The roentgenogram shows normal kidneys, but there was chronic pyuria, the cause of which was unknown. Malz briefly reviews the subject of renal infantilism. There are two theories: One suggests that the retardation of growth is due to loss of important minerals through the kidneys. The other suggests that both conditions exist coincidentally. Malz reports this case to suggest that retardation of growth may also result from chronic pyuria, even without hydronephrosis.

GERSTLEY, Chicago.

PRIMARY TUBERCULOSIS OF THE VULVA, IN ASSOCIATION WITH ERYTHEMA NODOSUM. A. NORDENSKJÖLD, Acta pædiat. **20**:257, 1937.

Accumulated clinical experience indicates that the tubercle bacillus rarely invades the body through the skin or through the mucous membranes; these serve as the portal of entry in probably not more than 0.1 per cent of all cases. A limited number of cases have been reported in which the primary focus was located in the skin, the tonsil, the gum or the middle ear of an infant. Although infection of the male genital organ during ritualistic circumcision is by no means rare, the occurrence of a primary focus in the vulva appears to be exceedingly uncommon. Approximately 11 authentic cases of this phenomenon have been reported; in 10 instances the patient was an infant or a child. The diagnosis is usually difficult, and the source of the infection generally evades unequivocal detection.

Nordenskjöld describes what she regards as the first case to be published in Sweden. The patient was a 6 year old girl who entered the hospital because of a week's illness, which consisted of fatigue, swelling of the lymph glands of both groins, and fever. The nodes were found to be slightly enlarged, tender, matted together and adherent to the overlying skin, which was reddened and edematous. Lesions were present which were characteristic of erythema nodosum. A purulent vaginal discharge was present. The Hamburger tuberculin test gave positive results, and the sedimentation rate of the erythrocytes was considerably accelerated. A few days after admission the vulva became conspicuously inflamed, and a small ulcer appeared near the orifice of the urethra. These manifestations subsided within a week; the lymphadenopathy receded without suppuration. Direct smears of the discharge from the vulva failed to aid diagnosis, but pus from the ulcer produced tuberculosis in guinea pigs, and tubercle bacilli of the human type were cultivated from the discharge. Treatment was limited to local hygienic measures. Four months later the local lesion had almost disappeared, and eighteen months after the beginning of the illness the patient was entirely well. Roentgenographic examination of the chest yielded negative findings; no tubercle bacilli were demonstrated in material obtained by gastric lavage. The correctness of the diagnosis in this case, as in others, is supported by (1) the character of the ulceration, (2) the subsequent appearance of tuberculous lymphadenitis of the regional nodes, (3) the appearance of erythema nodosum in chronologic association with the lesion and (4) the absence of evidence of tuberculous infection in other parts of the body. The bibliography is helpful.

MCCUNE, New York.

THE PROGNOSIS OF NEPHRITIS IN CHILDREN. K. DE LEEUW, Acta pædiat. (supp. 1, art. 2) **20**:1, 1937.

A review of the literature illustrates the difficulties which are encountered in obtaining information relating to the prognosis of nephritis in children. The use

of different systems of classification and the employment of different criteria in diagnosis make it well nigh impossible to collate the reports of the numerous writers who have dealt with this subject. The author tries with only moderate success to bring some order out of the chaos. In addition, he reports the results of follow-up examinations made some years after the original illness in 90 of 110 children who had been shown to have acute or chronic nephritis while in the Binnengasthuis, Amsterdam, Netherlands. Of 65 patients with acute nephritis, only 6 showed evidence of incurable, progressive disease; in 3 patients many months were required for recovery from the acute episode. Several patients were encountered who appeared to have chronic nephritis but who evidenced complete remissions after varying intervals of time. Three patients with pyelonephritis recovered completely. The author experienced difficulty in recognizing Heubner's paidonephritis and recommends that the term be abandoned. The nephrologist will find this paper useful, although the English is at times somewhat obscure. The point of view is objective.

McCune, New Yok.

Some Cases of Pyuria Treated by Sodium Mandalate. J. H. Smidt van Gelder, Maandschr. v. kindergeneesk. **7**:122 (Dec.) 1937.

Fourteen children aged from 4 weeks to 9 years who had chronic and acute pyuria were treated by means of sodium mandalate and ammonium chloride. The urine of 13 children was sterile after a treatment period of from five to twelve days. In the remaining child the treatment had to be stopped because of the appearance of renal and gastric irritation. Another child refused to take the drug. Three patients showed relapse; for 2 of them the cultures showed staphylococci and streptococci. No detrimental effects of the drug were seen.

van Creveld, Amsterdam, Netherlands.

Diseases of the Ductless Glands; Endocrinology

Traumatic Diabetes Insipidus. C. W. Rand and G. H. Patterson, Bull. Los Angeles Neurol. Soc. **2**:163 (Dec.) 1937.

Diabetes insipidus as a result of an injury to the head is uncommon. Rand and Patterson report 6 cases observed in private practice. All the patients were males, of ages varying from 10 to 24 years. Two were injured in automobile accidents and 2 by falls; 1 was kicked by a horse, and 1 was struck by a falling rock. In all cases the injury to the head was severe, being followed by unconsciousness, which in some cases lasted for several days. Fracture of the base of the skull was established by clinical or roentgen examination in 4 cases and was considered probable in the other 2. The intake of fluid varied from 4 to 9 liters, with a correspondingly elevated output of urine. Often the increase in water exchange was delayed in onset by the fact that the patient remained unconscious for days and hence could not demand fluid. In 2 cases this delay amounted to ten and fourteen days. Elevation of the blood sugar was not observed, and glycosuria did not occur in any case. One patient showed sharp bitemporal hemianopia, which was thought to be due to anteroposterior splitting of the chiasm. Another had a subdural hematoma over the right temporal region, which was removed surgically. A third patient had cerebrospinal rhinorrhea and a subsequent abscess of the right frontal lobe, for which operation was performed. This patient had generalized convulsive seizures. A solution of posterior pituitary was used in 3 of the 6 cases, with reduction in the urinary output. Complete recovery occurred in 4 of the 6 cases, in only 2 of which the solution of posterior pituitary was given. The recovery, apparently uninfluenced by this medication, required from three to six months. Partial recovery was observed in 2 cases for two and eight months, respectively. Other common sequelae of injury to the head, such

as headache and dizziness, were also observed in several cases. The diabetes insipidus was attributed to injury to the infundibular region of the brain.

MACKAY, Chicago. [ARCH. NEUROL. & PSYCHIAT.]

GENERALIZED OSTEITIS FIBROSA DUE TO A RETRO-ESOPHAGEAL PARATHYROID TUMOR. E. N. ALLOTT and J. JEMSON, Lancet **1**:609 (March 12) 1938.

Generalized osteitis fibrosa in a 19 year old girl, due to a parathyroid tumor, is described in order to emphasize the fact that the disease may reach a very advanced stage before being suspected. Although there was no obvious external deformity, roentgen examination showed widespread decalcification and cyst formaiton in numerous bones. After operation the metabolism of calcium and phosphorus returned to normal.

LANGMANN, New York.

DIABETES FROM LESION OF THE ANTERIOR LOBE OF THE PITUITARY AND ENDOCRINE PANCREATIC FUNCTION. B. A. HOUSSAY and V. G. FOGLIA, Rev. Soc. argent. de biol. **12**:237 (Aug.) 1936.

An alkaline extract of the anterior lobe of the hypophysis of the cow has a diabetic action on dogs. Extirpation of the liver brings about immediate lowering of the hyperglycemia due to the extract to a hypoglycemic level, a reduction which is not produced by injecting normal pancreas. It produces resistance to insulin so that when insulin is injected up to 2 units per kilogram the glycemia of the dogs given injections of the extract descends less and is more prolonged than in normal dogs or in dogs made diabetic by deficiency of the pancreas.

HERRON, Monroe, La.

THE WATERHOUSE-FRIEDRICHSEN SYNDROME. A. KAMBER, Monatschr. f. Kinderh. **71**:351 (Dec.) 1937.

Kamber reports a case of hemorrhage into the adrenal in a 2 year old boy, with the observations at autopsy. He reviews rather extensively the cases recorded since Marchand reported the first in 1880. The symptoms are due to adrenal insufficiency resulting from hemorrhage incidental to sepsis. The cardinal symptoms are a profound drop in blood pressure and in blood sugar, besides all the evidences of acute collapse. The condition usually terminates fatally in from six to eight hours (rarely the patient has lived as long as two days). The sepsis in a majority of cases is due to meningococcic infection. Occasionally streptococci have been found.

The treatment is that of acute adrenal insufficiency, with use of epinephrine, dextrose and glandular products.

GERSTLEY Chicago.

INVESTIGATIONS CONCERNING CONGENITAL STRUMA. O. BAADER, Ztschr. f. Geburtsh. u. Gynäk. **115**:445 (Sept.) 1937.

Congenital struma is not an inherited disease. It develops during intrauterine life in relation to the mother's constitution and is the first manifestation of the predisposition to have goiter. It occurs particularly in regions where goiters are endemic.

Congenital struma was found in 5.45 per cent of the population of upper Badenia, a German province. It occurs more frequently with increasing body length of the newborn and with increasing number of previous pregnancies of the mother. Congenital struma is seldom found in premature infants and is relatively frequent in large infants measuring more than 54 cm. at birth. Three per cent of the babies with congenital struma died from suffocation caused by the struma.

ADAIR and LANDÉ, Chicago.

THERAPY FOR DIABETIC COMA IN CHILDREN. H. HUNGERLAND, Ztschr. f. Kinderh. **59**:13 (Aug. 2) 1937.

Hungerland advocates energetic administration of insulin and fluids. The patient may be lost if treated too conservatively. One patient whose blood sugar was 1,000 mg. per hundred cubic centimeters was given 340 units of insulin in six hours; a second with a value of 1,100 mg. was given 475 units in nine hours, and a third with a value of 542 mg. was given 120 units in one hour. Two of the patients presented the symptom complex of boardlike rigidity of the abdomen and vomiting (simulating peritonitis) to which Linneweh and Bessan called attention.

SIEMSEN, Chicago.

Diseases of the Muscles, Bones, Joints and Lymph Glands

TOTAL MYELOSIS OF A FAMILIAL TYPE. A. ZUCCOLA, Pediatria **45**:243 (March) 1937.

Zuccola, after a careful review of the different theories as to the causes of the myeloses which involve the bone marrow functionally, describes 2 cases of globular myelosis of a familial type, probably congenital. He discusses the differential diagnosis among the various similar forms of myelosis and gives a short description of the therapy (by means of arsenic, iron and radium and in in some instances mercury).

PALMIERI, Brooklyn.

TREATMENT OF OSTEOMYELITIS. J. VALLS and C. E. OTTOLENGHI, An. Fac. de cien. de La Plata **1**:387, 1937.

Utilizing surgical treatment in cases in which the disease is acute, Valls and Ottolenghi vary their technic as follows: 1. Drainage for the subperiosteal abscess. 2. Trephining of the medullary space when the gross appearance of the bone suggests a focus of infection therein. 3. Resection of the diaphysis. 4. Amputation in adults in selected cases. After surgical treatment they resort to immobilization in plaster casts in accordance with Orr's method, especially in cases in which the disease has become chronic. In addition to surgical treatment, they employ vaccinotherapy, serotherapy, chemotherapy, intravenous injections of bacteriophage and on occasions blood transfusions. Their feeling is that these measures have no decisive action and deserve application only in conjunction with, and secondary to, surgical treatment. Their experience with diaphysial resection has not been good, and they justify amputation in patients in whom all other medical and surgical measures have failed to bring about improvement.

KALISKI, San Antonio, Texas.

A CASE OF PROGRESSIVE MYOSITIS OSSIFICANS. V. JORDANA and T. MARTY, An. de pediat. **11**:149 (March) 1935.

A girl of 4 years showed, starting at the fifteenth day of life, a bony swelling on the occiput, the size of a dove's egg, and subsequently multiple bony deposits in muscles of the neck, trunk and upper extremities, together with several exostoses, causing almost complete immobility of the affected parts. The pregnancy of the mother, the birth, diet and general development of the child and the family history are reported as normal. The Wassermann reaction of the blood was negative. The Mantoux test with a 1:1,000 dilution of tuberculin was negative. The blood calcium was from 13 to 16 mg., and the urinary calcium 20 mg., per hundred cubic centimeters.

Because of the high blood calcium parathyroid adenoma was suspected, and removal of such a tumor was attempted. However, the fixed flexion of the neck, with the chin almost touching the sternum, permitted isolation only of the lower

pole of the thyroid. The left inferior thyroid artery was ligated and severed in an attempt to cut off the blood supply of the parathyroids. The result was negative.

GIFFEN, Toledo, Ohio.

OSSEOUS DYSTROPHIES OF THE EXTREMITIES. F. J. ROCA, An. Soc. de puericultura de Buenos Aires **3**:103 (April-June) 1937.

Roca cites a case of agenesis or aplasia of the femur in a newborn infant. Etiologic factors include hereditary variations, syphilis, rickets, compression of the fetus in utero, debility, local inflammation and alcoholism. The treatment is operative.

HERRON, Monroe, La.

SOME CASES OF PSEUDARTHROSIS IN CHILDHOOD. P. SANCHEZ TOLEDO, Cir. ortop. y traumatol., Habana **4**:181 (July-Sept.) 1936.

The author describes in detail 4 juvenile cases of pseudarthrosis, which is a rare condition in children. His conclusions are: Every fracture ought to be treated adequately from the beginning, and strict vigilance is necessary until union is complete. A fracture of the diaphysis must be carefully examined to rule out interposition of the soft parts. Handling of the parts, as well as surgical intervention, requires the utmost caution in order to avoid damage to the vascularization of the fragments. Fractures of the olecranon, even with slight separation of the fragments, are not always a matter for surgical intervention. A fracture of the external condyle of the humerus with displacement of the fragments always requires a form of surgical treatment that permits repair of the rotation of the condyle.

Osteoplasty after Albee's method is the best means of treating pseudarthrosis.

HERRON, Monroe, La.

OSTEOMYELITIS OF THE MANDIBLE. A. BARBA INCLÁN, Cir. ortop. y traumatol., Habana **4**:205 (July-Sept.) 1936.

The author reports 2 cases of nonodontogenous osteomyelitis of the mandible. In the first, mandibular osteomyelitis followed a furuncle in a boy of 4 years. The histories and the surgical treatment in these cases are described in detail. Orr's method of treatment is generally followed in such instances.

HERRON, Monroe, La.

OSTEOGENESIS IMPERFECTA. L. PFAU, Rev. chilena de pediat. **8**:613 (Nov.) 1937.

Pfau presents a case of osteogenesis imperfecta in a premature infant. Such an occurrence is rare. The condition was diagnosed as a result of the finding of short extremities with normal hands.

Roentgenograms revealed curving of the long bones and subperiosteal fractures without cartilaginous lesions, thereby ruling out chondrodystrophy.

Pfau calls attention to the misnomer "fetal rickets" and to the inefficacy of antirachitic treatment.

The child died of bronchopneumonia at the age of 40 days.

SCHLUTZ, Chicago.

SPONDYLITIS CAUSED BY SAFETY PIN IN ESOPHAGUS. H. NAVIS, Ztschr. f. Hals-, Nasen- u. Ohrenh. **41**:159, 1936.

After reviewing the literature on safety pin in the esophagus, Navis reports an unusual case that was observed at the clinic in Leyden, Netherlands. A boy aged 3 was referred to the otorhinolaryngologic clinic by the orthopedic clinic, to which his parents had brought him on account of an extremely curved back. The roentgenogram of the vertebral column revealed an open safety pin apparently

in the esophagus, approximately at the bifurcation, at the level of the fifth and the sixth thoracic vertebra. These two vertebrae showed a spondylitic process and the question arose whether this process had a connection with the presence of the safety pin. Already at the age of 18 months the child had been examined at the orthopedic clinic because sitting up was difficult. At that time the vertebrae showed no lesions, but the safety pin was in the same position. However, no attention was given to it, probably because it was assumed that the pin, like several buttons which appeared in the roentgenogram, was in the clothing. In order to determine whether the spondylitis was caused by the safety pin, a new roentgenogram was made after a contrast medium had been introduced into the esophagus. The pointed part of the needle was behind the esophagus. It is assumed that the spondylitis had been caused by the inflammation, which, in turn, had been elicited by the perforation of the safety pin. It is peculiar that with the exception of the curved back the parents never noticed anything unusual. The child had always been able to eat everything and had never complained of pain. When told of the presence of the pin, the parents recalled that recently the child had not eaten properly and had repeatedly cried "pinprick." The pin was removed by esophagoscopic technic.

EDITOR'S ABSTRACT. [ARCH. OTOLARYNG.]

A CASE OF CONGENITAL CYSTIC LYMPHANGIOMA OF THE NECK IN AN INFANT. L. BRUNCLÍK JR., Časop. lék. česk. **75**:502 (May 1) 1936.

Brunclík reports in detail on a congenital cystic lymphangioma which was removed in toto from an infant at the age of 25 days. The operation was performed because of extreme interference with breathing and deglutition. The mass was the size of an adult male fist. Postoperative transfusion of 80 cc. of maternal blood was followed by uneventful recovery. The author discusses the various etiologic theories. The one usually accepted is that the condition arises from mechanical pressure during development, inflammatory, functional and embryonic. Photographs are presented.

STULIK, Chicago.

OCCURRENCE OF RHEUMATIC DISEASES AND OF CHRONIC ARTHRITIS DEFORMANS IN FINNISH CHILDREN. V. RANTASALO, Acta pædiat. **21**:297, 1937.

This report of statistics relating to the incidence of acute and chronic rheumatic disease in Finland contains no conclusions that can be profitably abstracted. As in America, acute rheumatic fever is more common and more malignant than chronic arthritis.

McCUNE, New York.

Diseases of the Eye

RECURRENT RETINOVITREOUS HEMORRHAGES IN THE YOUNG. P. BONNET, L. PAUFIQUE and L. SARAZIN, Arch. d'opht. **53**:849 (Dec.) 1936.

The authors first review the reports which have been published on this condition and comment briefly on the etiologic factors suggested. The question as to whether the hemorrhages are due to diapedesis or to rupture of a vessel is raised. Bonnet favors the idea of a slow breaking of the wall of the vessel. In relation to this the question of tuberculous periphlebitis is considered. A case is described in which changes were observed ophthalmoscopically prior to the appearance of hemorrhage, forecasting the hemorrhage, and also at the time of the hemorrhage. The late results of the hemorrhage were also noted. Colored plates illustrate the report. Active tuberculosis was shown clinically and bacteriologically. After extensive hemorrhage into the vitreous had cleared, definite areas of periphlebitis were found and are depicted. While many causes for this condition can properly be considered, most important is the presentation of complete clinical or anatomic observations made in cases of this kind.

S. MARLOW. [ARCH. OPHTH.]

CONGENITAL NYSTAGMUS AND DISTURBANCES OF NYSTAGMUS PROVOKED EXPERIMENTALLY. J. SÉDAN and G. E. JAYLE, Rev. d'oto-neuro-opht. **15**:529 (Oct.) 1937.

Those who have studied congenital nystagmus are in agreement on only one point: the absence of vestibular disturbance. Jayle and Grisoli (*Rev. d'oto-neuro-opht.* **15**:204 [March] 1937) reported a case of congenital nystagmus in which vestibular examination revealed anomalies. Two additional cases are now reported. The spontaneous nystagmus observed in these cases was characteristic as regards variability in rhythm, frequency and direction of the movements of the eyes. To this variability was added: extreme rapidity of the nystagmus, which became slower when the direction of gaze was changed; variability in the effect of convergence on nystagmus; transformation of the nystagmic movements by optical means; association of nystagmus with other disturbances of the ocular state, such as monocular vertical strabismus and associated head movements.

Vestibular disturbances are manifested under two forms: In the first group the provoked nystagmus is modified by the antagonism of the congenital and the provoked nystagmus. This effect varies from one patient to another. In the second group there appear anomalies in the results of the rotatory and galvanic tests, pointing, perhaps, to a central cause. Horizontal nystagmus is rarely disturbed. Provoked rotatory nystagmus is replaced by horizontal nystagmus; provoked vertical nystagmus is prolonged. These anomalies resemble those found in certain truncal lesions; they may even be traceable to anatomic anomalies of the pathways. DENNIS, San Diego, Calif. [ARCH. NEUROL. & PSYCHIAT.]

CONGENITAL CATARACTS. A. REBUFFO, An. agrupacion med. d. patronato de la infancia **1**:13, 1937.

The literature is reviewed and several classifications are given. In consideration of the etiologic factors, the author makes four observations: 1. In the embryologic development of the crystalline lens there may be a failure of absorption of the hyaloid artery. 2. A hereditary factor, although difficult to explain, cannot be denied. 3. Convulsions that shake the ciliary muscle may result in separation of the nucleus from the cortical substance. 4. A close relationship is to be noted between dental and ciliary nerves, with respect to which Benet stated ". . . in 22 of 25 instances of vascular cataract the teeth were diseased, malformed, rachitic, etc., the first molar being most diseased. The first molar is joined through nerve connections with the fibers which govern the ciliary epithelial processes for secretion of the nutritive liquids of the lens. Disturbances occurring at the moment of eruption of this diseased tooth may cause convulsions and other disturbance in the lens; also, the enamel of this tooth and the median layer of the lens form simultaneously, and any dystrophy rebounds equally on the two structures." This formation occurs, according to Griffith, at the sixth week of gestation. In conclusion the author accepts all the evidence of coincident lesions of teeth and of the thyroid and in general all lesions called rachitic and tetanic as factors but believes that these lesions are not the true cause, which he thinks is an intoxication. Along this line, he thinks, will be found the true solution in this interesting chapter of ophthalmology, about which the last word has not been spoken.

The treatment is surgical: extraction or iridectomy with extraction, according to type of cataract. GIFFEN, Toledo, Ohio.

COLOBOMA OF THE MACULA LUTEA IN MONOZYGOTIC TWINS: REPORT OF A CASE. K. VOGELSANG, Klin. Monatsbl. f. Augenh. **98**:322 (March) 1937.

Vogelsang reports in detail the cases of male twins aged 8 years, each with a coloboma of the right eye. Each boy showed mirror-like asymmetries of the fingers, ears, features, form of palate, teeth and tongue and various other struc-

tures. The father's eyes were normal in form and function except for irregular pupils, deep physiologic excavation of both disks and slight lighter discoloration of the temporal portion of the choroid. Vision was normal in each eye. The mother had juvenile glaucoma, which may have been correlated with the malformation of the right eyes of the twins. Vogelsang considers these colobomas malformations because of their concordant occurrence in monozygotic twins and because no further changes occurred in the fundi during eight years. The literature in point is cited.

STOLL, Cincinnati. [ARCH. OPHTH.]

OPHTHALMOMYIASIS INTERNA: REPORT OF A CASE. I. DERER, Klin. Monatsbl. f. Augenh. **98**:339 (March) 1937.

A boy aged 7 years had suffered from inflammation of his right eye for from six to seven weeks. It was caused by a larva of a fly, Wohlfartia magnifica (Sarkophaga), in the anterior chamber. The larva was about 7 mm. long and 1 mm. thick and consisted of nine segments. After extraction it coiled spirally. The vision was greatly reduced; the intraocular tension was increased to 60 mm. (Schiötz), and the lens was subluxated upward and toward the nose so that its lower margin appeared in the pupil. The eye became free from irritation soon after operation, and the vitreous cleared sufficiently for Derer to observe through the clear space below the lens that the disk was atrophic and that the retinal vessels were decidedly narrowed. Vision remained limited to perception and projection of light. The condition of the disk and retinal vessels led Derer to believe that the larva entered the eyeball by way of the blood stream. The sclera, which was intact in this case, would, however, have offered no obstacle to the entry of this kind of larva, which is known to pierce even sinews and bones.

STOLL, Cincinnati. [ARCH. OPHTH.]

ROENTGEN THERAPY OF RETINAL GLIOMA. H. SCHEYHING, Klin. Monatsbl. f. Augenh. **98**:756 (June) 1937.

The right eye of a boy aged 4 was enucleated for glioma, and the preoperative diagnosis was corroborated by histologic examination in November 1927. Shortly afterward the left eye was treated with roentgen radiation. Vision was 5/5 in the beginning of 1931, but radial opacities in the lens were observed by the end of that year. The cataract was extracted by another oculist in 1935, and a discission of a secondary cataract was performed by the author in December 1936. Illustrations show the difference in the appearance of the fundus in 1931 and in February 1937. The tumor, located above the disk, was greatly reduced and showed deposits of lime. Scheyhing was surprised to observe atrophy of the choroid surrounding the tumor and extending into the region of the macula; he considers it as a lesion due possibly to irradiation.

Four questions of importance are answered by the author in connection with this case. The diagnosis of glioma was confined by the histologic examination of the right eye and by the ophthalmoscopic examination of the left eye. Recovery actually occurred, as no recurrence was observed within ten years after roentgen irradiation. A case of the same duration of observation was reported by Heine.

It is impossible to decide whether recovery was the result of irradiation or whether it occurred spontaneously, as reported by a number of authors in cases in which the eyeball remained unaltered and vision was preserved. Scheyhing thinks that a glioma as small as that observed in the left eye of his patient may have offered a tendency for spontaneous recovery but that this tendency may have been stimulated by irradiation. Detrimental lesions as a result of irradiation were not observed, but slight changes in the conjunctiva and the cataract developed. The child received small doses, of from 30 to 50 per cent, during the first two years of his treatment, and two large doses, of 80 and 100 per cent, respectively, during the third and last year.

STOLL, Cincinnati. [ARCH. OPHTH.]

CONGENITAL ABSENCE OF ABDUCTION (CONGENITAL MUSCULAR STRABISMUS). C. V. LODBERG, Acta ophth. **15**:247, 1937.

This article surveys the entire subject of congenital absence of abduction and cannot be well abstracted. Seven of the author's cases are briefly reported and the symptoms tabulated. The symptomatology is discussed in some detail, consideration being given to such topics as absence of abduction, limitation of adduction of the same eye, retraction of the globe, narrowing of the palpebral fissure, elevation of the globe on attempting adduction, protrusion of the globe and widening of the palpebral fissure on attempting adduction, difference in motility obtained by covering the fellow eye, head turning and vertical motility.

The pathologic anatomy underlying these functional disorders is discussed, reference being made to many of the various muscular anomalies recorded in the literature. There are brief sections devoted to etiology and treatment. This article, 50 pages long, in French, is well worth perusal by those interested in the muscles. There is a bibliography of 90 references.

O. P. PERKINS. [ARCH. OPHTH.]

Skin Diseases; Allergy

INVESTIGATION OF VIRUS DISEASES OF SKIN, WITH REPORT OF CASE OF KAPOSI'S VARICELLIFORM ERUPTION. R. T. BRAIN and BEATRICE LEWIS, Brit. J. Dermat. **49**:551 (Dec.) 1937.

The authors discuss in a general way the difficulties inherent in the investigation of virus diseases. The clinical appearance of recognized virus diseases of the skin, although rather characteristic, is insufficient to incriminate a virus. Even inclusion bodies are not seen in all virus infections and when present are difficult to distinguish from products of granular degeneration in a cell. Elementary bodies are too small to be identified in tissue preparations, but when they can be separated by centrifugation their identity may be determined by an agglutination test with the patient's serum. The neutralization test and the complement fixation reaction sometimes give useful information. The neutralization test depends on the fact that a suspension of virus mixed with serum containing specific antibody loses its infective power or retains it in diminished degrees.

The authors report a case of Kaposi's varicelliform eruption in a boy aged 15. The disease ran a stormy course, and the boy died within two weeks after its onset. Cultures of the blood were sterile. Cultures of material from cutaneous lesions yielded Staphylococcus pyogenes aureus and a hemolytic pyogenic streptococcus. An attempt at autoinoculation with material from lesions failed. Inoculation of a guinea pig with such material produced lines of pus, and inoculation of a rabbit with the pus produced lesions, but histologic preparations of material from them showed no inclusion bodies. Tests of the rabbit serum for agglutinins, precipitins and neutralizing power against vaccinia virus all gave negative results. In short, all attempts to demonstrate the presence of a virus in this case or to show the relation of the disease to vaccinia failed. However, the lesions were well advanced before the investigations were begun, and the authors suggest that perhaps secondary infection accentuated the bacteriologic findings at the expense of a possible underlying picture of virus infection.

RATTNER, Chicago. [ARCH. DERMAT. & SYPH.]

PSYCHOTIC SYMPTOMS IN A CASE OF ACRODYNIA. G. HEUYER, ROUDINESCO and VENDRYES, Rev. neurol. **68**:840 (Dec.) 1937.

A 10 year old boy had for six months shown psychic changes, gradually becoming worse. Mental confusion and delirium were present. Shortly after admission to the hospital he began to show swelling and redness of the hands. Ulcerations appeared on the backs of the hands, which healed and desquamated.

The pulse rate was 76; the blood pressure, 90 systolic and 70 diastolic. The spleen was enlarged. The reflexes were normal, and there was no hypotonia. Lumbar puncture gave negative results.

(Although the authors assume that this was acrodynia, pellagra seems a more plausible diagnosis.)

DAFFINEE, Boston.

MECHANISM OF THE ACTION OF "RAW DIET" IN INFANTILE ECZEMA. N. CARRARA, Lattante **8**:607 (Nov.) 1937.

Carrara claims that the diet which he used, when well tolerated, gives excellent results in eczema. The diet is high in carbohydrate and vitamin and low in fat, sodium chloride and water; also, complete elimination of milk and eggs is desirable.

HIGGINS, Boston.

CERTAIN FACTORS CONTRIBUTING TO THE FREQUENCY OF ECZEMA. E. J. VIRASORO and F. UGARTE, An. Soc. de puericultura de Buenos Aires **3**:71 (April-June) 1937.

The authors find that there is a difference in the frequency of eczema in different years and in different seasons. They also find that eczema is more prevalent when barometric pressure is high (i. e., humidity) and that these physical factors predispose to an exudative diathesis.

HERRON, Monroe, La.

HIGH FAT FEEDINGS IN THE ECZEMATOID INFANT (SECOND COMMUNICATION). J. DAMIANOVICH and A. M. CORDIVIOLA, An. Soc. de puericultura de Buenos Aires **3**:84 (April-June) 1937.

The authors have previously reported 30 cases, and now add 14 new cases, of infantile eczema and seborrhea in which treatment was by the use of a diet high in fat. The fat percentage was from 6.4 to 6.5, and the authors used the formula of Dr. Gaing. They do not believe that the high fat formula is harmful to the eczematous infant but have found it to be of great value in the treatment of infantile eczema and seborrhea. It cured or benefited all of their patients.

HERRON, Monroe, La.

INFANTILE ACRODYNIA. A. M. VEGA DE GANDOLFO HERRERA, Rev. méd. latino-am. **23**:310 (Dec.) 1937.

Acrodynia was studied for the first time in an epidemic in Paris in 1828. It was described in North America in 1919 and, without knowledge of earlier work on the disease, was thought to be a new disease. In the present article the characteristic symptoms are reviewed and the following clinical forms described: (1) the nervous form, in which motor, sensory and psychic disturbances predominate, and there are few or no cutaneous symptoms; (2) the cutaneous form, in which nervous symptoms are lacking or terminal; (3) the gangrenous form, very rare, with grave trophic changes; (4) the "ganglionic" form, with tachycardia and transitory psychic, pruritic and asthenic symptoms; (5) the ocular form, with psychic symptoms, erythroderma, conjunctivitis and intense photophobia, and (6) the "ganglionic form" in which tachycardia and hypertension are characteristic.

The principal points in the differential diagnosis are given, as well as the changes found at necropsy. The causative agent is probably a neurotropic virus. The treatment is symptomatic.

DWYER, Kansas City, Mo.

OSSEOUS FORM OF RECKLINGHAUSEN'S DISEASE. G. RATELL and O. USINGER, Rev. Soc. de pediat. de Rosario **2**:195 (Oct.) 1937.

In the 10 year old boy presented, besides the cutaneous manifestations, there was hypertrophy of the skull in the frontal area. This is well shown by roentgenograms. This made a noticeable asymmetry of the face.

SANFORD, Chicago.

SERUM SICKNESS AND THE HEART. A. A. KOLTYPINE, J. Ukranian Sc. Inst. Maternal & Child Health, 1937, p. 16.

One of the most frequent cardiac troubles in patients with acute toxic infections is a biphasic syndrome of the vegetative nervous system. The cardiac syndrome is most clearly marked in the clinical picture of severe diphtheria and is the usual cause of death. It is just at the moment when the cardiac disturbance develops that the collateral influence of serum sickness is met.

If serum therapy is necessary, precautions should be taken so far as possible to avoid serum disease, particularly in the selection of a more refined, concentrated type of serum.

SEMENENKO-MCKHANN, Boston.

Miscellaneous

ROENTGEN THERAPY IN INFLAMMATORY AND INFECTIOUS LESIONS. B. C. CUSHWAY and R. J. MAIER, Illinois M. J. **72**:517 (Dec.) 1937.

The authors report on 329 patients with infection and inflammation treated by irradiation during the past two years. Their results show that certain kinds of infections are particularly susceptible to the action of the roentgen rays. In some instances (furuncles, carbuncles, metastases, parotitis, erysipelas, Ludwig's angina) the response seems almost specific. The acute infections are the most responsive. Chronic infections are less susceptible and require repeated treatment.

BARBOUR, Peoria, Ill.

DISTRIBUTION OF SULFANILAMIDE IN THE ORGANISM. E. K. MARSHALL JR., KENDALL EMERSON JR. and W. C. CUTTING, J. Pharmacol. & Exper. Therap. **61**:196 (Oct.) 1937.

A study was made on dogs. After administration of sulfanilamide the drug was present in approximately equal concentrations in the various tissues with the exception of bone and fat. Simultaneous determinations of sulfanilamide in the blood and spinal fluid of man during several hours' administration of the drug shows that the concentration in the spinal fluid is parallel to and slightly lower than that in the blood.

PILCHER, Cleveland.

SYNERGISM OF ETHYL ALCOHOL AND SODIUM PENTOBARBITAL. J. M. DILLE and R. P. AHLQUIST, J. Pharmacol. & Exper. Therap. **61**:385 (Dec.) 1937.

Two separate observers had reported that alcohol antagonized the narcotic (and lethal) dose of phenobarbital in the rabbit and had proposed alcohol as a remedy for such poisoning. A third observer found that when ethyl-butyl barbituric acid and alcohol were given at the same time to rats the action of each was markedly potentiated. The authors, wisely questioning the ability of one narcotic to act as an antidote to another, investigated the action of alcohol and pentobarbital sodium, alone and combined, in 120 experiments on 48 rabbits. They found no antagonistic action but marked synergism of action and conclude that alcohol has no place in the treatment of acute barbituric acid poisoning.

PILCHER, Cleveland.

MOTIVES IN CHOOSING VOCATIONS. W. CWEIGENHAFT, Zycie Mlodych **7**:54 (Feb.) 1938.

In analyzing children between 8 and 12 years of age, the author found that 50 per cent want to be soldiers, aviators and the like, because of patriotic and adventurous motives. About 40 per cent want to follow trade because the work

is clean and pays well. Only a few want to be in business. From the foregoing observations the author comes to the conclusion that life has greater influence on one's choice of vocation than school.

KRUPINSKI, Chicago.

TRANSFUSION OF PRESERVED BLOOD IN EARLY INFANCY. E. M. TOURTCHINA, Pediatriya, 1937, p. 20.

Febrile reactions were more marked and occurred more frequently following transfusion of preserved blood than following that of fresh citrated blood. The transfusion of preserved blood may be indicated in infants for chronic infections accompanied by progressive loss of weight. In the treatment of grave dystrophies accompanied by secondary anemia only fresh citrated blood should be used.

SEMENENKO-McKHANN, Boston.

BOTULISM IN NETHERLANDS. A. J. R. E. VAN SCHOONHOVEN VAN BEURDEN and A. CLARENBURG, Nederl. tijdschr. v. geneesk. **81**:6024 (Dec. 18) 1937.

This is a description of the symptoms of an intoxication with the toxin of Bacillus botulinus (type B) occurring in a family of 6 persons (2 adults and 4 children). The necessity of the antiserum being available early is stressed. The principal symptoms in the described cases were disturbances in the reactions of the pupils and in the accommodation and dryness of the mouth. The intoxication followed use of infected ham. In 2 patients specific toxin could be demonstrated in the blood. An investigation of the spinal fluid of 5 patients for toxin disclosed none.

VAN CREVELD, Amsterdam, Netherlands.

INFLUENCE OF SLEEPING DRUGS ON THE COMPOSITION OF THE BLOOD. C. D. DE LANGE, Nederl. tijdschr. v. geneesk. **82**:3560 (July 16) 1938.

Two patients, after the use of hypnotic drugs, were found to show in their blood two phenomena, namely, hyperlipemia, indicating marked disturbance in fat metabolism, and slight to moderately severe anemia. De Lange subsequently confirmed these observations in animals, in which she found that with several hypnotics very considerable changes could be brought about in fat metabolism and that, likewise, anemia could be produced.

VAN CREVELD, Amsterdam, Netherlands.

Book Reviews

Säuglingskrankheiten. By. Prof. Dr. Heinrich Finkelstein. Fourth edition. Price, 13.50 florins. Pp. 890, with 204 illustrations. Amsterdam: Elsevier, 1938.

This is the fourth and presumably the last edition of the greatest work ever written on diseases of nurslings. It resembles former editions in length and general arrangement, though many chapters have been rewritten, and more American references have been included. There are six divisions: (1) development and feeding of nurslings, (2) disturbances during the transition from fetal to extrauterine life, (3) disturbances involving actual change in the composition of the body (nutrition, etc.), (4) metabolic diseases, (5) general infections and (6) diseases of individual organs.

The book opens and closes an epoch in pediatrics. Thirty years ago Finkelstein and Meyer announced their studies on alimentary intoxication, at a time when students of infant nutrition groped, helpless and bewildered, for leadership. These thirty years have seen methods and theories of infant nutrition so simplified that mortality resulting from improper feeding is practically unknown today. This tremendous gift to humanity is largely due to the life-long studies of Finkelstein himself.

He modestly reminds pediatricians, however, that they need take no great pride in their accomplishments. He recalls that dilution of milk with the addition of carbohydrate or fat and the use of sour milk are actually only modifications of technics already used. The success of physicians is negative rather than positive. They have learned what not to do. They do not injure the baby with too great quantities of food. They avoid one-sided mixtures. They have no fear of protein. They know enough of vitamins to understand the success of empiric diets. But Dr. Finkelstein feels that the real problem of infant nutrition still lies untouched. Why does the breast-fed infant possess far greater immunity to infection than the one who is artificially fed? Those who have followed Dr. Finkelstein's studies will be interested in his revised classification of nutritional disease. He has introduced several changes.

The book occupies a niche of its own in the pediatric library. Representing the life experience of one of the greatest pediatric clinicians, this is no ordinary school book, to be skimmed over lightly, but rather an encyclopedia. Rarely may a single person possess so unlimited an opportunity for the study of infants, so comprehensive a brain and such energy to record thoughts and observations as Dr. Finkelstein. The book stands as a monument to his studies. It should be in the library of every pediatrician who considers his specialty as more than a liaison between high pressure commercial detail men and patient.

Le diagnostic radiologique des tumeurs malignes du pharynx et du larynx. By F. Baclesse, chief of staff of the Curie Foundation; preface by A. Hautant. Price, 100 francs. Pp. 270, with 236 illustrations. Paris: Masson & Cie, 1938.

This is virtually an atlas, beautifully illustrating the detail of anatomic structure of the neck as seen in roentgenograms. Those showing the altered contours and densities of the larynx and pharynx are supplemented in many instances by drawings, which point out the details. The topography of normal anatomic structures is outlined against abundant evidence of proved pathologic changes. There are descriptions of special roentgen technic designed to bring out the detail of soft tissue for the study of the mechanism of phonation as well as altered contours which result from infections or from benign or malignant neoplasms. The author places considerable emphasis on the character of the margins of a mass. Diffuse

densities are more likely to be the result of malignant invasion, as compared with the homogeneously dense, sharp demarcated outline of a benign growth. Granulomatous changes of tuberculosis and syphilis may resemble neoplastic infiltrations. Dr. Baclesse has had an unusually large experience with comparative roentgen examinations following high voltage roentgen therapy, and he conclusively demonstrates the value of recording regressions of tumors in serial roentgenograms. In some instances roentgen examination depicts retropharyngeal pathologic change more clearly and accurately than routine examination, but for the most part it can be considered only as a supplementary procedure which will occasionally demonstrate involvements to be considerably greater than is evident by direct examination alone. The marvelous illustrations accurately portray the varied manifestations of malignant neoplastic infiltrations.

This splendid outline will serve as a valuable reference for any one contemplating further efforts along these lines. The book is written in French in a pleasing manner and is easy to read.

Babies Are Human Beings. By C. Anderson Aldrich, M.D., and Mary M. Aldrich. Price, $1.75. Pp. 128, with 5 illustrations. New York: The Macmillan Company, 1938.

The authors have discussed the psychologic aspects of the baby's life and of his training in good habits from a practical point of view.

It is obvious that they have had intimate personal experience with children. The material indicates that many problems which confront the parents of a baby may be met with success. The discussion of the scientific basis for training furnishes adequate reasons for the directions given. The illustrative case histories tend to emphasize and clarify the advice. Throughout the book there is keen appreciation of the differences between individual babies. The right of each baby to his own variation within the normal pattern of development is clearly recognized.

Both mothers and fathers will benefit by reading this book. It will also be useful for teachers and could be read with profit by most physicians.

The Premature Baby. Children's Bureau, United States Department of Labor. Paper. Pp. 12. Washington: United States Government Printing Office, 1938.

This small pamphlet describes the bed, clothing, feeding and general care of the premature infant. It contains no information that is not presented much better in any pediatric textbook. The purpose of the book is not apparent. Certainly it is of no use to the doctor; perhaps it is intended for the laity. A doctor's care for all premature infants would seem better than a pamphlet to parents.

Pediatric Symptomatology and Differential Diagnosis. By Sanford Blum, M.D. Price, $5. Pp. 500, with 29 illustrations and 1 color plate. Philadelphia: F. A. Davis Company, 1938.

All the usual diseases of children, including the exanthems, are considered. Symptoms and differential diagnosis are discussed exhaustively, while etiology, pathology and treatment are purposely omitted. The diseases are grouped in their natural sequence and are described in a running narrative, which makes easy reading.

This excellent book is well written and pleasingly printed.

Dr. Colwell's Daily Log for Physicians. Twelfth edition. Price, $6. Champaign, Ill.: Colwell Publishing Company.

The 1939 edition of this useful account book has all the admirable features which have characterized the former editions.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini 24, Rome, Italy.
Secretary: Professor Vitetti, Rome, Italy.
Place: Boston. Time: Sept. 9-12, 1940.

American Committee:
Chairman: Dr. Henry F. Hemholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. Kenneth Blackfan, 300 Longwood Ave., Boston.

Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St., W., Montreal.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

British Paediatric Association

President: Dr. Hector C. Cameron, 23 Devonshire Pl., Upper Wimpole St., London, W. 1.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava.
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Sociedad Cubana de Pediatría

President: Dr. Clemente Inclan Costa, Manrique 48, Habana.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

Société de Pédiatrie de Paris

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. Edward Clay Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: Hotel Chase, St. Louis. Time: May 15-19, 1939.

American Academy of Pediatrics

President: Dr. H. F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Netherland Plaza Hotel, Cincinnati. Time: May 16-18, 1939.
Region I. Place: Waldorf-Astoria Hotel, New York. Time: June 1-3, 1939.
Region II. Place: Nashville, Tenn. Time: May 15-16, 1939.
Region IV. Place: Oakland, Calif. Time: April 6-8, 1939.

American Hospital Association, Children's Hospital Section

Chairman: Miss Mabel Binner, Children's Memorial Hospital, Chicago.
Secretary: Winifred Culbertson, Children's Convalescent Hospital, Cincinnati.

American Pediatric Society

President: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: Skytop Lodge, Skytop, Pa. Time: April 27-29, 1939.

Canadian Society for the Study of Diseases of Children

President: Dr. R. R. MacGregor, 142 Wellington St., Kingston, Ontario.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, Hospital for Sick Children, Toronto.

Society for Pediatric Research

President: Dr. L. Emmett Holt Jr., Johns Hopkins Hospital, Baltimore.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

North Pacific Pediatric Society

President: Dr. Frederick Fischer, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. C. L. Lyons, Paulsen Medical-Dental Bldg., Spokane, Wash.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Charles E. Conrad, 209-210 Professional Bldg., Harrisburg, Va.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.

INTERMOUNTAIN PEDIATRIC SOCIETY

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 837 Boston Bldg., Salt Lake City.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Hyman Green, 483 Beacon St., Boston
Secretary-Treasurer: Dr. Henry E. Gallup, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. John Schoonover, Republic Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

STATE

ALABAMA PEDIATRIC SOCIETY

President: Dr. Stewart H. Welch, 1117 S. 20th St., Birmingham.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.
Place: Montgomery. Time: April 17, 1939.

ARKANSAS STATE PEDIATRIC ASSOCIATION

Chairman: Dr. G. D. Murphy, 112 Peach St., El Dorado.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.
Place: Hot Springs. Time: January 1939.

CALIFORNIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

Chairman: Dr. Harold K. Faber, 2341 Clay St., San Francisco.
Secretary: Dr. Hartzel H. Ray, 23–2d Ave., San Mateo.

FLORIDA STATE PEDIATRIC SOCIETY

President: Dr. Gilbert S. Osincup, 300 E. Colonial Dr., Orlando.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Coral Gables.
Place: Concurrent with state association meeting at time of convention.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Charles Hall Farmer, 553 Walnut St., Macon.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.
Scientific Meeting—Place: Augusta. Time: Jan. 12, 1939.
Business Meeting—Place: Atlanta. Time: April 1939.

HEZEKIAH BEARDSLEY PEDIATRIC CLUB OF CONNECTICUT

President: Dr. C. V. Calvin, 144 Golden Hill St., Bridgeport.
Secretary: Dr. E. T. Wakeman, 129 Whitney Ave., New Haven.
Time: Three meetings a year.

INDIANA STATE PEDIATRIC SOCIETY

President: Dr. O. N. Torian, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

IOWA PEDIATRIC SOCIETY

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.
Secretary-Treasurer: Dr. Philip C. de Verges, 312 Audubon Bldg., New Orleans.

MEDICAL SOCIETY OF STATE OF NEW YORK, SECTION ON PEDIATRICS

Chairman: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester.
Secretary: Dr. Leslie O. Ashton, 842 Park Ave., New York.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA, PEDIATRIC SECTION

Chairman: Dr. John M. Higgins, 600 S. Wilbur Ave., Sayre.
Secretary: Dr. John D. Sturgeon Jr., 22 N. Gallatin Ave., Uniontown.

MICHIGAN STATE MEDICAL SOCIETY, PEDIATRIC SECTION

Chairman: Dr. Allan L. Richardson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. Ward L. Chadwick, 524 Medical Arts Bldg., Grand Rapids.

MISSISSIPPI STATE PEDIATRIC SOCIETY

President: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by society. Time: Yearly.

NEBRASKA PEDIATRIC SOCIETY

President: Dr. Herman M. Jahr, 1120 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. Elmer W. Bantin, 440 Aquila Court Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

NORTH CAROLINA PEDIATRIC SOCIETY

President: Dr. W. Myers Hunter, 306 N. Tryon St., Charlotte.
Secretary: Dr. J. R. Adams, 412 N. Church St., Charlotte.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. Ben H. Nicholson, 301 W. 12th St., Oklahoma City.

SOUTH CAROLINA PEDIATRIC SOCIETY

President: Dr. Mylnor W. Beach, 126 Meeting St., Charleston.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

TENNESSEE STATE PEDIATRIC SOCIETY

President: Dr. William E. Van Order, 546 McCallie Ave., Chattanooga.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Jackson. Time: April 11, 1939.

TEXAS PEDIATRIC SOCIETY

President: Dr. F. O. Calaway, 3306 Fannin St., Houston.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Houston. Time: May 9, 1939.

VIRGINIA PEDIATRIC SOCIETY

President: Dr. W. Ambrose McGee, 616 W. Grace St., Richmond.
Secretary: Dr. John M. Bishop, Medical Arts Bldg., Roanoke.

WEST VIRGINIA STATE MEDICAL SOCIETY, SECTION ON PEDIATRICS

President: Dr. J. L. Blanton, 207 Fairmont Ave., Fairmont.
Secretary: Dr. Theresa O. Snaith, 450 Center Ave., Weston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. N. C. Wetzel, 2103 Adelbert Rd., Cleveland.
Secretary: Dr. Fred Rittenger, 10515 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto, Canada.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto, Canada.

Bronx Pediatric Society

President: Dr. Samuel T. Levethan, 254 E. 184th St., Grand Concourse, New York.
Secretary: Dr. David Greene, 910 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Benjamin Kramer, 6 Pierrepont St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank van der Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. Joseph K. Calvin, 2376 E. 71st St., Chicago.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. Harold Nesbit, 1719 Pacific Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. William O'Donnell, 1553 Woodward Ave., Detroit.
Secretary: Dr. Robert Mason, 5140–2d Blvd., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

District of Columbia Medical Society, Pediatric Section

President: Dr. Harry H. Donnally, 1612 I St., N. W., Washington, D. C.
Secretary-Treasurer: Dr. Harry A. Spigel, 2647 Connecticut Ave., Washington, D. C.
Place: District Medical Society. Time: 8 p. m., fourth Thursday of each month from October to April, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. L. H. Goldsmith, 384 Peachtree St., N. E., Atlanta.
Secretary: Dr. James P. Hanner, 384 Peachtree St., N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. John K. Glen, 4412 Montrose Blvd., Houston, Texas.
Secretary-Treasurer: Dr. J. L. Collier, 1620 Medical Arts Bldg., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Urban Busiek, 200 E. Pershing St., Springfield, Mo.
Secretary: Dr. Fred Speer, 2700 Parallel Ave., Kansas City, Kan.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. H. R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Paul M. Hamilton, 248 E. Main St., Alhambra, Calif.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Sidney D. Kramer, 61 Eastern Parkway, Brooklyn.
Secretary: Dr. Benjamin Stoloff, 1149 Eastern Parkway, Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. James Dobbins, 42-04 Ditmars Blvd., Long Island City, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144–38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Memphis Pediatric Society

President: Dr. Barton Etter, 376 S. Bellevue St., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. Joseph Shimpa, 2309 N. 36th St., Milwaukee.
Secretary: Dr. Helen Jane Zillmer, 781 N. Jefferson St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Secretary: Dr. Lucy Porter Sutton, 168 E. 74th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Robert Rosenthal, 437 Lowry Medical Arts Bldg., St. Paul.
Secretary-Treasurer: Dr. R. E. Nutting, 205 W. 2d St., Duluth, Minn.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Every month, except June, July and August.

Philadelphia Pediatric Society

President: Dr. Julian M. Lyon, 40 Llanfair Rd., Ardmore, Pa.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to June, inclusive.

Richmond Pediatric Society

President: Dr. A. S. Hurt, 1028 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. Louise Fry Galvin, 2416 Stuart Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month, except July, August and September.

Rochester Pediatric Society

President: Dr. J. Merrel Parker, 11 N. Goodman St., Rochester, N. Y.
Secretary: Dr. H. C. Soule, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

St. Louis Pediatric Society

President: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Secretary-Treasurer: Dr. Peter G. Danis, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society Bldg. Time: Third Friday of each month from September to June.

Seattle Pediatric Society

President: Dr. Jay I. Durand, 1305–4th Ave., Seattle.
Secretary: Dr. Frederick B. Joy, 1215–4th Ave., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Secretary: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Clement Smith, 1101 Beacon St., Brookline, Mass.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.
Place: Horace H. Rackham Graduate School, Ann Arbor, Mich. Time: Nov. 11-12, 1938.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. Norman Survis, 650 Main St., New Rochelle.
Secretary-Treasurer: Dr. Elvira Ostlund, 131 Purchase St., Rye.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.